

Editor in Chief IRVING S. WRIGHT, M.D.
Consulting Editor RICHARD H. ORR, M.D.

Pseudomonas Aeruginosa Infections

By **CLAUDE E. FORKNER, JR., M.D.**

Assistant in Medicine, Cornell University
Medical College, New York, N.Y.
Formerly Assistant in Medicine, Harvard
Medical School, Formerly Chief, Allergy
and General Medicine Branch, National
Cancer Institute, National Institutes of
Health, Bethesda, Maryland



GRUNE & STRATTON • 1960

NEW YORK AND LONDON

Contents

PREFACE

1 CHARACTERISTICS OF <i>PSEUDOMONAS AERUGINOSA</i>	1
Bacteriology	1
Endotoxins	1
Pigments	2
Antibiotic Activity	3
Serology and Immunity	3
Epidemiology	3
Pathogenicity	5
2 CLINICAL MANIFESTATIONS OF INFECTION	6
Septicemia	6
Granulocytopenia and Thrombocytopenia	11
Bacterial Endocarditis	12
Cyanosis	15
Burn	18
Meningitis	19
Respiratory Infection	36
Catheteritis	39
Genitourinary Tract	43
Pseudomonas Infection Associated with Pregnancy	4
Osteomyelitis and Arthritis	50
Eye	59
Ear	60
Meningoencephalitis	63
3 ANTIBIOTIC THERAPY	64
Systemic Infection	6
Local Infection	6
Intrathecal Administration	6
Oral Administration	66
Topical Administration	66
Meningoencephalitis	66
Therapy with Colistin Salt	67
4 PATHOLOGY	69
Septicemia	71
Pneumonia	74
INDEX	101

The manuscript of this volume was awarded
HONORABLE MENTION
in the second Modern Medical Monographs Competition.

Copyright © 1900 by Crune and Stratton, Inc.
381 Park Avenue South New York 16 New York
Library of Congress Catalog Card Number 60 15123
Printed and Bound in the United States of America (B)

Preface

SUPERINFECTIONS CAUSED BY antibiotic resistant bacteria are commonplace. With the advent of new drugs which alter the balance of bacterial flora and with the development of new therapeutic measures such as organ transplantation and chemotherapy of cancer requiring the suppression of natural body defense mechanisms the threat of resistant infections has become paramount.

Infections due to *Pseudomonas aeruginosa* in their every form are sufficiently uncommon that many physicians do not have wide experience in their diagnosis and management. Many important contributions have dealt with single case reports or isolated experiences; many others are available only in foreign journals and foreign languages. It is with these issues in mind that the present comprehensive review of pseudomonas infections was undertaken.

The author's personal experience has been limited for the most part to those infections developing in the setting of malignant disease; however, it is evident that many of the lessons learned will be applicable whatever the underlying disease process will be. A report of clinical experience with septicemia due to *Pseudomonas aeruginosa* has previously been published.¹⁴⁰

The clinical data have been presented so that different systems of the body are dealt with separately. Within each section insofar as possible reports have been discussed chronologically. It is hoped that this will represent the most effective way of presenting the available information.

Many hundreds of references were scanned in compiling the present bibliography. The references included are believed to be representative, pertinent, and up to date.

The author wishes to express his deep appreciation to Dr. C. Gordon Zubrod, Clinical Director, National Cancer Institute, Bethesda, Maryland, for his encouragement and constructive criticism. A particular debt of gratitude is owed to Dr. John Edgcomb, Department of Pathology, National Institutes of Health, Bethesda, Maryland, who had the major responsibility for the section

To Kate

on pathology and for the photographs. Finally the many helpful suggestions offered by Dr Maxwell Finland Associate Professor of Medicine Harvard Medical School and Associate Director Thorn-
dike Memorial Laboratory Boston Massachusetts are gratefully
acknowledged

CLAUDE E FORBNER JR M D

1 *Characteristics of Pseudomonas Aeruginosa*

BACTERIOLOGY

Pseudomonas aeruginosa (*B. pyocyaneus* *Ps. pyocyanea* *B. aeruginosum*) is a slender rod shaped actively motile flagellated gram negative bacterium with rounded ends. Its stated dimensions are 1.5 to 3.0 micra in length and 0.5 micron in breadth. Frequently it grows in short chains of two or more organisms. The number and position of flagellae may vary within a given strain.¹⁷ The organism is aerobic and does not form spore. It forms acid from glucose but from no other sugar.^{3, 10, 18, 20} Growth occurs at temperatures ranging from 5 to 42 C. The optimal growth temperature is 37 C.¹⁷ The bacteria grow in large spreading colonies which may vary morphologically. Gelatinous variants exist.^{8, 13, 27}

Classification of strains under the genus *Pseudomonas* is difficult because of their variety and wide range of activity. Criteria for their separate identification are unsettled. *Ps. aeruginosa* is the only member of the genus known to be pathogenic for humans. A laboratory test for the identification of *Ps. aeruginosa* based on the high intracellular concentration of cytochrome oxidase and the formation of indophenol blue has been described.^{1, 4} Good reviews of bacteriologic studies of *Ps. aeruginosa* are available.^{1, 15, 14, 19}

ENDOTOXINS

Filtrates of broth cultures of pseudomonas have demonstrated proteolytic activity.^{11, 16} Likewise potent endotoxins have been identified. Pyromen (formerly Pyrogen) is a purified cell free product obtained from pseudomonas³ which has been used in fever therapy³¹ and in the study of pyrogenic reactions. In 1950 Bennett

This manuscript was based on work done while the author was with the General Medical Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.

1 *Characteristics of Pseudomonas Aeruginosa*

BACTERIOLOGY

Pseudomonas aeruginosa (*B. pyocyaneus*, *Ps. pyocyanea*, *B. aeruginosum*) is a slender rod-shaped actively motile flagellated gram-negative bacterium with rounded ends. Its stated dimensions are 1.5 to 3.0 micra in length and 0.5 micron in breadth. Frequently it grows in short chains of two or more organisms. The number and position of flagellae may vary within a given strain.¹² The organism is aerobic and does not form spores. It forms acid from glucose but from no other sugar.^{3, 9, 2, 1} Growth occurs at temperatures ranging from 5 to 42 C. The optimal growth temperature is 37 C.^{4, 12} The bacteria grow in large spreading colonies which may vary morphologically. Gelatinous variants exist.^{8, 4, 9}

Classification of strains under the genus *Pseudomonas* is difficult because of their variety and wide range of activity. Criteria for their separate identification are unsettled. *Ps. aeruginosa* is the only member of the genus known to be pathogenic for human. A laboratory test for the identification of *Ps. aeruginosa* based on the high intracellular concentration of cytochrome oxidase and the formation of indophenol blue has been described.^{13, 4} Good reviews of bacteriologic studies of *Ps. aeruginosa* are available.^{1, 1, 13, 11}

ENDOTOXINS

Filtrates of broth cultures of pseudomonas have demonstrated proteolytic activity.^{11, 4, 6} Likewise potent endotoxins have been identified. Piromen (formerly Pyromen) is a purified cell-free product obtained from pseudomonas³ which has been used in fever therapy^{3, 15} and in the study of pyrogenic reactions. In 1950 Bennett

This monograph based on work done while the author was with the General Medicine Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland.

and Beeson³ published a comprehensive review of pyrogen. The most potent known pyrogens appear to be those associated with the somatic antigens of gram negative bacteria.^{33, 40, 41}

The physiologic disturbances produced by endotoxins were reviewed in 1954 by Thomas⁴² and a syndrome of vascular collapse was described.⁴³ Several clinical and experimental reports pertain to the mechanism of this state.^{33, 41, 44, 45, 46, 47} Experimentally no qualitative difference in action or effect has yet been found between the endotoxin of *Ps. aeruginosa* and that of other gram negative bacteria. Progressive illness and eventual death occurs in some patients whose blood has been rendered sterile by antimicrobial agents. This is in accord with the concept that the pathologic effects of pseudomonas infection are not so much those of living bacteria as of their toxic products. One endotoxin of gram negative bacteria consists of phospholipid and polysaccharide moieties sometimes associated with protein or polypeptide.^{47, 48} Landy⁴³ has demonstrated that removal of protein from such a complex does not alter the biologic characteristics of the endotoxin.

PIGMENTS

The best known pigment of *Ps. aeruginosa* is pyocyanin, a deep blue phenazine derivative⁴⁹ soluble in both chloroform and water.⁴¹ It was first isolated from cultures of pseudomonas in 1860 by Fordos.¹³ The relatively innocuous effect of pyocyanin on human skin and leukocytes has been investigated.⁵⁰ Pyocyanin constitutes a reversible oxidation-reduction system and acts as a respiratory catalyst. It has been termed the major respiratory enzyme of *Ps. aeruginosa*.⁵¹ Pyocyanin formation is specifically inhibited by certain respiratory poisons (KCN) which suggests that respiratory enzymes are involved in pyocyanin biosynthesis.⁵² Other pigments may be formed.⁴¹⁷ Many strains lose the ability to form pigment apparently irreversibly,¹⁵³ and many original isolates are nonpigmented.^{1, 153, 167, 168}

Bacterial fluorescence of *Ps. aeruginosa* has been reported.²⁷⁴ This characteristic has been used clinically⁸⁸ as well as in the identi-

fication of culture. Chromatographic investigations have been described by Rivera cited by Williams^{4, 5} who thought that classification of strains on the basis of pigment formation ultimately might be useful.

ANTIBIOTIC ACTIVITY

Substances with antibiotic activity have been isolated from extracts of *Ps. aeruginosa*^{4, 115, 1, 136, 3}. Methods for the production, purification, and isolation of some of them have been described^{146, 443, 444}. These antibiotics have been variously attributed to enzymes, pigments, and endotoxins. Activity against typhoid fever^{4, 3}, diphtheria¹, *E. coli*^{4, 9}, *M. tuberculosis*¹¹⁵, viruses¹⁴, fungi^{3, 134}, and gram positive bacteria have at one time or another been described.

SEROLOGY AND IMMUNITY

Pseudomonas infection induces production of agglutinin. A titre higher than 1:30 is rarely encountered in a normal person, but titres of 1:1000 or higher may occur during systemic infection¹¹⁰. Neter and Weintraub^{3, 1} suggest the use of the conditioned bacterial hemagglutination test to differentiate actual infection from carrier state. This test seems to offer greater sensitivity than the conventional bacterial agglutination test; it depends on the ready adsorption of the somatic antigens of *Ps. aeruginosa* by erythrocytes which are then specifically agglutinated by homologous bacterial antibodies. Gaines and Landy^{1, 4} have demonstrated in random human sera the presence of *Ps. aeruginosa* hemagglutinins in the absence of bacterial agglutinins; this suggests that man must come in contact with and develop an immunologic response to *Ps. aeruginosa* more frequently than is generally appreciated.

EPIDEMIOLOGY

Ps. aeruginosa is widely distributed in nature. The percentage of people who are carriers of *pseudomonas* in the intestinal tract has been variously estimated from 0.04 to 15.5 per cent^{87, 1, 9}.

^{1, 9} Studies on the epidemiologic features of *pseudomonas* infec-

and Beeson³ published a comprehensive review of pyrogen. The most potent known pyrogens appear to be those associated with the somatic antigens of gram negative bacteria.^{413 414 415}

The physiologic disturbances produced by endotoxins were reviewed in 1954 by Thomas⁴¹² and a syndrome of vascular collapse was described.⁴¹⁴ Several clinical and experimental reports pertain to the mechanism of this state.^{39 42 11 10 181} Experimentally no qualitative difference in action or effect has yet been found between the endotoxin of *Ps. aeruginosa* and that of other gram negative bacteria. Progressive illness and eventual death occurs in some patients whose blood has been rendered sterile by antimicrobial agent. This is in accord with the concept that the pathologic effects of pseudomonas infection are not so much those of living bacteria as of their toxic products. One endotoxin of gram negative bacteria consists of phospholipid and polysaccharide moieties sometime associated with protein or polypeptide.^{463 464} Lindy⁴⁶³ has demonstrated that removal of protein from such a complex does not alter the biologic characteristics of the endotoxin.

PIGMENTS

The best known pigment of *Ps. aeruginosa* is pyocyanin, a deep blue phenazine derivative⁴¹⁶ soluble in both chloroform and water.⁴¹⁷ It was first isolated from cultures of pseudomonas in 1860 by Fordos.¹¹⁹ The relatively innocuous effect of pyocyanin on human skin and leukocytes has been investigated.⁸ Pyocyanin constitutes a reversible oxidation reduction system and acts as a respiratory catalyst. It has been termed the major respiratory enzyme of *Ps. aeruginosa*.⁴¹⁸ Pyocyanin formation is specifically inhibited by certain respiratory poisons (KCN) which suggest that respiratory enzymes are involved in pyocyanin biosynthesis.¹⁹¹ Other pigments may be formed.⁴¹⁷ Many strains lose the ability to form pigment apparently irreversibly¹²² and many original isolates are nonpigmented.^{1 103 107 8}

Bacterial fluorescence of *Ps. aeruginosa* has been reported.⁷¹ This characteristic has been used clinically⁸⁶ as well as in the identi-

fication of cultures Chromatographic investigations have been described by Rivera cited by Williams^{4, 5} who thought that subclasi fication of strains on the basis of pigment formation ultimately might be useful

ANTIBIOTIC ACTIVITY

Substances with antibiotic activity have been isolated from extracts of *Ps aeruginosa*^{4, 115, 1, 136, 37} Methods for the production purification and isolation of some of the e have been described^{196, 443, 444} These antibiotics have been variously attributed to enzymes pigments and endotoxins Activity against typhoid fever^{4, 3} diphtheria¹ *E coli*^{4, 9} *M tuberculosis*¹⁰⁰ viruses¹⁴ fungi^{3, 134} and gram positive bacteria have at one time or another been described

SEROLOGY AND IMMUNITY

Pseudomonas infection induces production of agglutinins A titre higher than 1:30 is rarely encountered in a normal person but titres of 1:1000 or higher may occur during systemic infection¹⁰ Netter and Weintraub^{3, 7} suggest the use of the conditioned bacterial hemagglutination test to differentiate actual infection from carrier state This test seems to offer greater sensitivity than the conventional bacterial agglutination test it depends on the ready adsorption of the somatic antigens of *Ps aeruginosa* by erythrocytes which are then specifically agglutinated by homologous bacterial antibodies Gaines and Landy¹ have demonstrated in random human sera the presence of *Ps aeruginosa* hemagglutinins in the absence of bacterial agglutinins this suggests that man must come in contact with and develop an immunologic response to *Ps aeruginosa* more frequently than is generally appreciated

EPIDEMIOLOGY

Ps aeruginosa is widely distributed in nature The percentage of people who are carriers of *pseudomonas* in the intestinal tract has been variously estimated from 0.04 to 15.5 per cent^{57-8, 1}
^{17, 2} Studies on the epidemiologic features of *pseudomonas* infec

tion are available^{176 96 7 358} Recent observations emphasize the adaptability of pseudomonas organisms to all kinds of liquid media including antiseptic solutions^{6a 6b 86 345} as well as urine bottles and bed pans³⁰ Transmission may occur by way of contaminated hands of ward personnel³⁰ since infections are largely confined to hospitalized patients Revealing studies on the prevention of

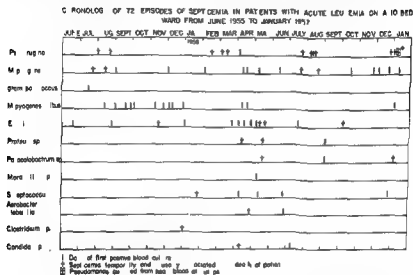


FIG 1 — Illustration of grouping of generalized *Pseudomonas* infections in contrast to more random distribution of other infections on a leukemia ward (From Forkner et al *Pseudomonas septicemia* *Am J Med* 23: 87, 1958 Reprinted by permission of the publisher)

P. aeruginosa infections in irradiated mice and rats have been reported⁴⁴⁴ Widespread infection originated from carriers and was propagated by fecal contamination of drinking devices Elimination of the causes controlled the epidemic In our own experience pseudomonas septicemia has occurred in several small epidemics in patients with acute leukemia treated on the same ward¹⁴⁰ This was in contrast to the more random temporal distribution of other infections as indicated graphically in FIGURE 1 Epidemics have been noted elsewhere^{345 349}

PATHOGENICITY

In 1850 Sedillot demonstrated the transferability of greenish blue discolorations on surgical dressings.³⁴ Lucke in 1862³⁵ showed that this condition was infectious and saw rod shaped elements in the discharge. In 1882 Gessard¹⁶³ obtained *Ps aeruginosa* in pure culture from two cutaneous wound discolored blue green. Gruber¹⁸⁴ in 1887 recovered *Ps aeruginosa* from green suppurations of the ear. Despite early demonstration by Charrin⁶ in 1889 of pathogenicity for animals recognition of the pathogenicity of this organism for man was not immediate.

In regard to *Ps aeruginosa* Ford quotes Schimmelbusch³⁷

While it can cause local inflammation and general symptoms it never invades the body at least in adults. Oler³³⁴ in reference to *Ps aeruginosa* wrote: "Although this is not a frequent cause of septicemia and pyemia it nevertheless deserves special mention. It is probably not an independent pathogen but occurs only as a secondary invader in existing lesions—especially of the mouth and skin. As shall be illustrated given the proper predisposing circumstances there is scarcely a region of the body exempt from infection with *Ps aeruginosa*."

2 *Clinical Manifestations of Infection*

SEPTICEMIA

Since Finkelstein¹ in 1896 first reported blood cultures positive for *Ps. aeruginosa* it has become firmly established that this organism may produce septicemia. Although Finkelstein is generally credited with the first ante mortem report of pseudomonas septicemia, Williams and Cameron⁴⁴ in 1893 and 1894 observed two children with typical courses; post mortem cultures were positive for pseudomonas from the internal organs in one and from the heart blood in the other. They termed the disease "cyanopyaemia." Their observations were not printed until 1896 because of a delay in transit to the publisher. These writers in turn credited Ehlers²¹³ in 1890 with isolation (post mortem) of pseudomonas from the blood and organs of similar cases. As a result of systematic bacteriologic study of 800 consecutive autopsies at the Johns Hopkins Hospital, Barker¹ in 1897 was able to find 11 cases of either local or general pyocyanic infection. A severe hemorrhagic tendency and a high incidence of smooth muscle paralysis were noted in these cases.

The pathogenicity of pseudomonas for animal had already been noted⁴. In his treatise *La Maladie Pyocyane*, Charrin presented a summary of the pathogenicity of pseudomonas in rabbit¹⁰¹. The pathogenicity of pseudomonas in dogs was described by Cuderc⁵ in 1890.

Lartigau⁶ in 1896 reported three cases of pseudomonas infection in man and described the clinical evolution of "maladie pyocyane." Characteristic features of septicemia were reported to be irregular fever, vasomotor disturbances, focal necroses and hemorrhagic lesions in the parenchyma of various with a predilection for the small bowel. A high incidence in children was noted. The following year Brill and Libman⁴⁶ reviewed the literature and

reported the first adult patient with pseudomonas septicemia. Pigmented spots were noted over the body; the possible relationship of the π to circulating toxic factors was considered.

In 1901 Waermann⁴ reported an epidemic of 11 newborn infants with umbilical infections terminating in fatal pseudomonas septicemias. Most of the π patient had pulmonary disease. Babes¹³ also recorded a case of pseudomonas septicemia which originated in the umbilicus.

Waite⁴ in 1907 reviewed the literature and added two cases. Fraenkel^{144, 147} in four monographs written between 1906 and 1925 discussed at length and in great detail the histopathologic changes associated with generalized pseudomonas infection. In particular he described the characteristic appearance of pseudomonas lesion in the skin and blood vessels which is said to be pathognomonic of infection by this organism. To quote directly: "The anatomic basis for all the organic changes of pyocyanus infection is to be sought in a characteristic typical colonization of the bacilli in the walls of the blood vessels in the diseased foci and in the locally induced disturbance in nutrition increased by toxic influence. This finding even without the cultural identification of the bacilli permits of an anatomic diagnosis of pyocyanus infection. Examples of this feature are shown in FIGURES 2 and 3."

Dold^{1 + 136} in 1918 and 1919 reported a relationship of pseudomonas infection to a typhoid-like fever locally known as Shanghai fever or 13 day fever. The illnesses were associated with splenomegaly and a roseola-like maculopapular skin exanthem; they resembled typhoid or paratyphoid fever in their clinical picture and course. Usually in the absence of complications patients became afebrile in two or three weeks. Pseudomonas was isolated from the blood, urine, feces, and skin; repeated attempts to isolate or agglutinate typhoid or paratyphoid organisms were unsuccessful. Lilley and Bearup⁷⁹ in 1928 described 9 patients with generalized pseudomonas infection originally thought to be typhoid fever. The organism was cultured from the blood in 2 (possibly 4) of the 9 cases. The authors were also impressed by leukocytosis as a differentiating diagnostic feature distinct from typhoid fever. The viru-

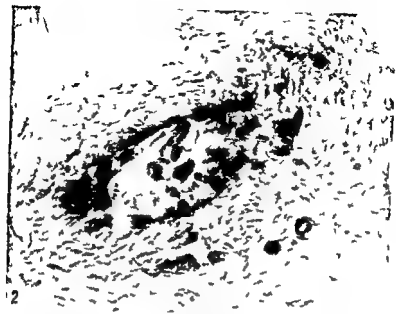


FIG 2—(above) *Pseudomonas* vasculitis, submucosal connective tissue in H&E (×1100)

FIG 3—(below) *Pseudomonas aeruginosa* in and near the wall of capillaries, subcutaneous adipose tissue in H&E (×1500)

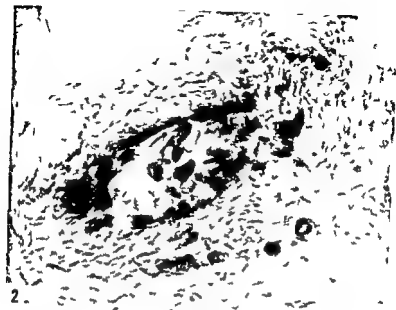
lence of the bacteria was considered to be increased by passage from patient to patient.

Epstein and Croman¹¹⁹ in 1933 emphasized the potential virulence of *Pseudomonas* in children particularly in infants as compared to adults. They reported a 7 year old child with a history of abscesses in the axillary and anogenital regions who had an 18-day course of fever and rectal pain associated with icterus, splenomegaly, purpura, thrombocytopenia, leukopenia, agranulocytosis, rapidly spreading infection and death. Ante mortem cultures of the blood and stool were positive for *Pseudomonas*. At autopsy the characteristic gross and microscopic lesions of *Pseudomonas* infection were found throughout the body. Examination of the tibial marrow revealed many fat cells, absence of myeloid cells and very few megakaryocytes.

Stanley¹²⁰ in 1917 reviewed the literature and reported 5 cases with terminal septicemia. One of these had bacterial endocarditis. Kerby³⁶ reviewed 83 reported cases of *Pseudomonas* septicemia. Of 39 cases in children the apparent portal of entry was the gastrointestinal tract in 25.7 per cent, the skin in 15.1 per cent and the middle ear in 12.6 per cent. In 44 cases of infection in adults septicemia occurred after operative procedures in 31.9 per cent—most commonly after urologic procedures.

Keefler and Hewitt¹²¹ as part of a program designed to evaluate the therapeutic effectiveness of streptomycin collected by 1948 a series of 3,000 infections treated in the United States. Of these there were 19 patients with *Pseudomonas* septicemia. The portal of entry were the urinary tract in 8 cases, skin wounds in 4 cases, the upper respiratory tract in 1 case. In 5 cases the primary focus was unknown. There were 10 deaths, a fatality rate of 53 per cent.

Mirabel¹²² in 1952 over a period of 11 months collected 18 cases of septicemia due to *Pseudomonas* from the pediatric department of San Juan City Hospital. With the exception of one 10 year old child all patients were younger than 16 months. Diarrhea was the original complaint in 61 per cent of the cases and in these the gastrointestinal tract was assumed to be the portal of entry. Other apparent sources were otitis media 11 per cent, umbilical cord 5.5



2.



3

FIG 2—(above) *Pseudomonas* in culture, submucosal connective tissue mouth Hematoxylin eosin ($\times 1100$)

FIG 3—(below) *Ps. aeruginosa* in and near the walls of capillaries subcutaneous adipose tissue abdomen Hematoxylin eosin ($\times 1500$)

accounted for approximately one half 12 patients had septicemia due to *Ps aeruginosa* 6 pseudomonas infections were thought to have originated from the genitourinary tract (5 following cystitis 1 from the skin and 5 from unknown focus) All had fever and 8 had chills Two had metastatic abscesses Thrombocytopenia occurred in 2 cases and agranulocytosis in 1 of the 6 Of the 12 patients 2 had ecthymatous lesions None of 3 patients who received polymyxin B died however 1 patient who received only tetracycline died

During the years 1954 through 1956 23 cases of septicemia due to *Ps aeruginosa* occurred at the Clinical Center of the National Institutes of Health The great majority of the 23 patients had acute leukemia Of the 23 cases 22 were fatal and all of the 23 were autopsied Observations on this series with illustrations of the more important clinical and pathologic features have been reported¹⁴⁰

GRANULOCYTOPENIA AND THROMBOCYTOPENIA

Brill and Libman⁴⁶ in 1899 reported 2 cases of pseudomonas septicemia and remarked on the absence of leukocytosis despite a fulminating infection Gheroghiewsky⁴⁷ the same year claimed to have found a leukocyte destroying ferment in cultures of pseudomonas In 1906 Rolly⁴⁸ among other early writers stressed the presence of hemorrhagic diatheses and abnormal coagulability of the blood in these infections Freeman¹⁴¹ in 1916 postulated a leucocidin as responsible for the leukopenia Hirszfild et al⁴⁹ in 1948 described 14 infants with pseudomonas infection 9 of whom died The authors were frequently able to culture pseudomonas from aspirated tibial or femoral marrow when blood cultures were negative They associated granulocytopenia and thrombocytopenia with involvement of the bone marrow Lovett⁵⁰ found that injections of pseudomonas could reduce the leukocyte count of guinea pigs and cause degeneration of leukocytes in the peritoneal cavity Lanthicum⁵¹ in 1927 Dasse⁵² in 1928 and Delatour⁵³ in 1932 injected pseudomonas into animals intravenously and observed that the bacterium or its products apparently caused granulocytopenia by destroying granulocytes or by inhibiting their formation

per cent post operative or post instrumental 5.5 per cent unknown 11 per cent Symptoms and signs in order of frequency were fever 83.4 per cent diarrhea vomiting skin lesions cyanosis edema jaundice (16.6 per cent) hepatomegaly and splenomegaly Agranulocytosis and thrombocytopenia were not observed The overall mortality was 67 per cent Polymyxin B was not used

Martin and co workers⁴⁹ in 1954 reported 10 cases of septicemia due to *Ps. aeruginosa* encountered at the Mayo Clinic over a period of 13 years All the patients had fever usually of a high spiking type and 7 of the 10 had chills One patient had thrombocytopenia and developed necrotic lesions on the buttock Another had a large erythematous lesion of the thigh leukopenia thrombocytopenia and jaundice The portal of entry was the genitourinary tract in 7 cases Of the patients 3 who had serious associated conditions died Polymyxin B was not used

Hoffman and Finberg⁵⁰ suggest that a very humid environment contributed to the increasing incidence of pseudomonas infections noted in their nursery Of 13 infants with pseudomonas infection 3 developed septicemia and died and 2 others with local infections died Only 3 of the 13 had received antibiotics prior to infection All were treated with polymyxin B

Koch⁴⁴³ in 1956 reported studies on 50 instances of septicemia due to gram negative bacteria of the opportunist pathogen group occurring since 1951 All the patients were men and all had received some form of chemotherapy prior to the onset of septicemia Six patients with pseudomonas septicemia died One patient infected by both *E. coli* and *Ps. aeruginosa* and treated with tetracycline survived Portals of entry in the 6 cases were urinary tract 3 intestinal tract 1 respiratory tract 1 skin 1 All of the pseudomonas septicemias were of sudden onset and five were preceded by instrumentation

Spittel and co workers⁴⁰³ in 1956 reviewed all cases of bacteremia due to gram negative bacteria exclusive of cases of typhoid fever brucellosis and bacterial endocarditis that were treated at the Mayo Clinic between 1940 and 1954* Of 137 cases collected *E. coli*

* This series included patients reported earlier by Martin et al.⁴⁹

accounted for approximately one half. 12 patients had septicemia due to *Ps. aeruginosa*. 6 pseudomonas infections were thought to have originated from the genitourinary tract (5 following cystoscopy, 1 from the skin and 5 from unknown foci). All had fever and 8 had chills. Two had metastatic abscesses. Thrombocytopenia occurred in 2 cases and agranulocytosis in 1 of the 6. Of the 12 patients, 2 had ecthymatous lesions. None of 3 patients who received polymyxin B died; however, 1 patient who received only tetracycline died.

During the years 1954 through 1956, 23 cases of septicemia due to *Ps. aeruginosa* occurred at the Clinical Center of the National Institutes of Health. The great majority of these patients had acute leukemia. Of the 23 cases, 22 were fatal and all of them were autopsied. Observations on this series with illustrations of the more important clinical and pathologic features have been reported.¹⁴⁰

GRANULOCYTOPENIA AND THROMBOCYTOPENIA

Drill and Libman¹⁴¹ in 1899 reported 2 cases of pseudomonas septicemia and remarked on the absence of leukocytosis despite a fulminating infection. Cheroglowsky¹⁴² the same year claimed to have found a leukocyte destroying ferment in cultures of pseudomonas. In 1906 Rolly¹⁴³ among other early writers stressed the presence of hemorrhagic diatheses and abnormal coagulability of the blood in these infections. Freeman¹⁴⁴ in 1916 postulated a leucocidin as responsible for the leukopenia. Hirsfeld et al.¹⁴⁵ in 1918 described 11 infants with pseudomonas infection, 9 of whom died. The authors were frequently able to culture pseudomonas from a pirated tibial or femoral marrow when blood cultures were negative. They associated granulocytopenia and thrombocytopenia with involvement of the bone marrow. Lovett¹⁴⁶ found that injections of pseudomonas could reduce the leukocyte count of guinea pigs and cause degeneration of leukocytes in the peritoneal cavity. Linticum¹⁴⁷ in 1927, Daise¹⁴⁸ in 1929 and Delitour¹⁴⁹ in 1932 injected pseudomonas into animals intravenously and observed that the bacterium or its products apparently caused granulocytopenia by destroying granulocytes or by inhibiting their formation.

More recently Hubbard and co workers ¹¹ have described experiments wherein a strain of pseudomonas recovered from the intestinal tract of an infant was introduced into mice and rabbits and produced the characteristic necrotic lesions. They also noted preferential disintegration of granulocytes when blood cells were exposed in vitro to a mixture of pseudomonas and proteus organisms. They postulate a capacity of pseudomonas to inactivate leukocyte proteolytic enzymes in order to explain the coagulative type of necrosis produced by the organisms. Markley and co workers ⁹ recently studied pseudomonas septicemia in Peruvian patients with burns and found that although the leukocyte count was usually in the normal range if the course was rapidly fatal there was leukopenia or if the course was prolonged before death there was leukocytosis.

Many other reports have dealt with the relationship of agranulocytosis to infection with *Ps. aeruginosa*.^{1, 5, 9, 10, 11, 12, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100}

BACTERIAL ENDOCARDITIS

Bacterial endocarditis is a rare manifestation of infection with *Ps. aeruginosa*. At least 20 cases have been reported. Some information about the cases is recorded in Table 1. In some instances the diagnoses appear certain; in other cases (5, 6, 12, 14, 17) diagnoses seem uncertain. In at least 11 patients the mitral valve was involved.

TABLE 1—Reported Cases of Endocarditis Due to *Ps. Aeruginosa*

Author	Patient	Valve	Remarks
Barker ¹⁶ (Thayer) ^{4, 1}	41 F	Mitral	Portal probably intestinal tract. Pseudomonas cultured from mitral vegetation, omentum, and bowel.
Blum ²¹	21 mo M	Mitral	Congenital syphilis. Focus of infection unknown. Pseudomonas obtained in pure culture from vegetations.
De la Camp ⁹	51 F	Mitral	Skin probably portal of entry. Blood culture negative prior to death. Pseudomonas cultured from heart blood and mitral valve.

Another possible case was not translated up to the time of publication.^{4, 6}

TABLE 1—Continued

Author	Patient	Valve	Remarks
Rolly ²	28 F	Mitral	Bowel probably portal of entry Pseudomonas recovered from spinal fluid and blood before and after death Also cultured from vegetations
Buncler	65 M	Mitral	Patient had RHD with mitral insufficiency Treated with Saproctin (in Pseudomonas) There was endocarditis of mitral valve with perforation No positive blood culture obtained Vegetation not cultured
Ka	35 M	Aortic Mitral	Portal of entry skin abscess Pseudomonas cultured from blood and urine before death. Not cultured after death Had typical histologic changes of endocarditis Bacteria in aorta and pulmonary artery
Fletcher ²²	41 M	Aortic	Pseudomonas septicemia—probably from urinary tract Gram negative rods in saline vegetations Kidneys and aorta involved.
Merue and Anderson	66 M	Mitral	Pseudomonas septicemia in diabetic with RHD Portal probably urinary tract Had mitral stenosis Pseudomonas cultured from vegetations
Staley	45 M	Tricuspid	Pseudomonas septicemia following Pneumococcus VII septicemia Pseudomonas cultured from valve Treated with sulfapenillin and a tetracycline
DeMeth and Rawlin	40 M	Aortic	Pseudomonas septicemia from intestinal tract Treated with streptomycin and pyoanaph
Hill ²⁴	28 F	Tricuspid	History of rheumatic fever age 8 Pulmonary Pseudomonas septicemia Acute bacterial endocarditis at necropsy Treated with penicillin streptomycin polymyxin
B	19 F	No proof	Autopsy revealed only Pseudomonas in spinal fluid flow, abscess No demonstrated septicemia

TABLE 1—Continued

Author	Patient	Valve	Remarks
Coller and Dyer ⁷⁸	53 F	Aortic Mitral	Lung probably primary site. No previous known valve damage. <i>Pseudomonas</i> cultured from blood, urine, feces and throat before death. Smears and cultures of vegetations positive. Multiple antibiotics.
Kenoyer et al. ²³⁵	20 M	No proof	History of RHD since age 7, with valvular damage. <i>Pseudomonas</i> septicemia. Recovered with neomycin.
Waldren and Hastings ⁴³¹	81 M	Mitral	History of RHD. Blood cultures positive before and after death. Smears and cultures of vegetation positive for <i>Pseudomonas</i> . Treated with multiple antibiotics.
Brundon et al. ⁹	37 F	Mitral	Remittent fever 1 week after mitral commissurotomy with <i>Pseudomonas</i> in blood and sputum. Died 9 weeks after valvulotomy. <i>Pseudomonas</i> cultured from lungs, abscess, bone marrow, valve vegetation.
Gottgegen and Romoda ¹	18 M	No proof	Four year course of endocarditis with history of polyarthritis and defective heart valve. <i>Pseudomonas</i> cultured from blood and urine during last 6 months. Cured by plenelectomy after resistant to all tried antibiotic.
Curtin et al. ⁷	26 F	Aortic	No history of RHD or known previous murmur. Developed fever, chills. 4 blood cultures were positive for <i>Pseudomonas</i> . Developed <i>Abhitula</i> after operation for ectopic pregnancy which probably became infected at time of cystoscopy 2 months prior to death.
McDonald et al. ²³¹	23 M	Aortic Mitral Tricuspid	Narcotic addict with recurrent rheumatic fever. Blood cultures positive before and after death. Culture of vegetation positive for <i>Pseudomonas</i> . Multiple antibiotics.

TABLE 1—Continued

Author	Patient	Remarks
Tetel and Florman ⁴	14 F	Patient was febrile 20 weeks after corrective surgery for patent ductus and interatrial septal defect. Recurrent fever. Chills. Polyphagia. Many blood cultures positive for pseudomonas. Intermitting postoperative blood cultures despite prolonged antibiotic administration including high dosage of polymyxin B. Reoperation disclosed a 2½ cm silk suture dangl in the right atrium removed by clamping of <i>Ps. aeruginosa</i> . Following excision of this perforative course was begun and the patient recovered.

in 3 of these there was associated involvement of the aortic valve. The aortic valve alone was affected in 3 cases and the tricuspid valve alone in 2 others. Positive blood cultures were never obtained in 2 of the less certain cases. Liedberg¹ mentioned without detail the occurrence of acute endocarditis in 4 burned patients whose ante mortem blood cultures were positive for pseudomonas. In 3 of these patients at least one other organism was cultured from the blood.

CUTANEOUS LESIONS

Many and varied descriptions of cutaneous lesions attributed to pseudomonas appear in the literature among which are the following: petechiae¹¹¹ roseola like^{104, 106} maculopapular¹⁴ infiltrative⁷ hypertrophic⁴⁰⁹ simulating leprosy⁹ erythelasma like cellulitis⁴ erythema multiforme like⁴¹ erythema nodosum⁴² exfoliative¹⁸⁰ pellagra like¹⁰ hemorrhagic³⁷⁰ vesicular⁴⁴⁷ bullous¹¹⁴ multiple ecthyma^{3, 8} pemphigoid^{107, 317} pustular³⁴³ ulcerative^{1, 11} gangrenous^{1, 471} necrotic⁷⁸. Some of this apparent variation may be attributed to the natural morphologic evolution of the lesion in its various stages of maturity.

Lesions beginning as macules or vesicle later becoming bullous

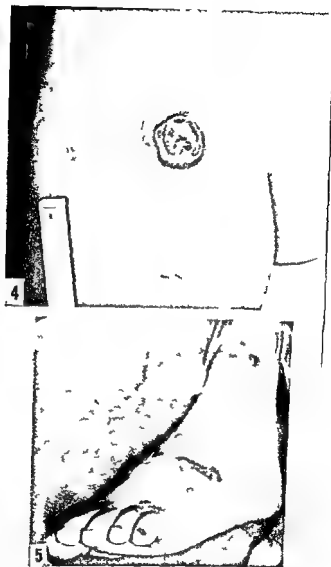


FIG 4—(above) Characteristic appearance of ecthyma gangrenosum. Note the black coagulative necrotic center and umbilicated margin. Inflammatory reaction minimal.

FIG 5—(below) Characteristic appearance of *Pseudomonas* cellulitis vesicular form. One vesicle has ruptured and is assuming an umbilicated ecthymatous appearance. (From Forkner et al: *Pseudomonas septicemia*. *Am J Med* 25:87, 1958. Reprinted by permission of the publisher.)



6

FIG. 6.—Extensive necrotic ulcerated areas on the buttocks and back of this 13 year old girl with acute yellow fever. The lower hemorrhagic thoracic lacerations on the right side are also a result of the same organism were cultured from the ulcerations.

or pustular and eventually sloughing to form gangrenous ulcers already observed by Ehlers¹¹³ and others were described by Barker¹ in 1897 and considered by him to be cutaneous manifestations of systemic pseudomonas infections. Hirschman and Kreibich⁹ the same year gave to the lesions the name of ecthyma gangrenosum. Robinson²⁶³ referred to the dermatologic manifestations of pseudomonas septicemia as "Characteristic" and consisting of profuse cutaneous hemorrhages that tend to suppurate and become gangrenous—preceded by initial vesicles that develop in petechiae and purpuric macules. Ecthyma like crusted areas are the result of this morphologic change.

Ecthyma gangrenosum. A pustular eruption usually associated with a hardened base and surrounded by an inflammatory area. The pustules develop large black spots (pigmented necrotic) on the 47

A typical cutaneous lesion starts as an erythematous macule often in the anogenital area which rapidly becomes vesicular containing a cloudy opaque cent fluid from which the organism may be cultured. The lesion may exist singly or in clusters. The surrounding tissue is inflamed and tender. Following rupture a circular hard dark crusty core develops. This is characteristically surrounded by a narrow rim of erythema. There is little or no evidence of inflammation peripherally and the lesion is non tender. The histologic changes are similar to those of pseudomonas lesions elsewhere in the body. Variations in the form of flattened hemorrhagic well demarcated areas of cellulitis may occur. The vesicular stage may be absent. Illustrative lesions are shown in FIGURES 1-6.

In our own series of patients the onset of septicemia in a few cases was preceded or accompanied by the appearance of pink round or oval maculopapular plaques on the trunk measuring up to two centimeters in diameter. These were evanescent and their relationship to systemic infection or to the previously described cutaneous lesions uncertain. Seeding of the blood stream from cutaneous lesions is probably common and the reverse process occurs in some cases.

Bauer and Cohen¹⁰ have described with colored illustrations 4 cases of infection of fingernail with *Ps aeruginosa* as the primary offender. *Candida albicans* was also present in 3 of the 4. They found the most effective treatment to be 0.1 per cent polymyxin B sulfate in 1 per cent acetic acid followed by 2 per cent methylrosaniline. Other reports of infected fingernails are available.^{17, 310} Howe¹⁴ described invasive infection of the leg due to pseudomonas, this was successfully treated with surgical debridement and topical 10 per cent urethane solution.

BURNS

With the advent of antibiotics a reduction in the incidence of gram positive bacterial contamination of burns was achieved. However, no comparable effect has been noted for burns contaminated with *Ps aeruginosa*. Jackson et al.¹¹ in 1951 (at the Burn Re-

surgery Unit of the Birmingham Accident Hospital found that in burned patients pseudomonas was responsible for more fatal chest complications and septicemia than any other organism. The local application of 0.1 per cent polymyxin significantly reduced the incidence of contamination of burns with pseudomonas and promoted the healing of graft. Other studies^{15, 16} have shown that secondary infection with pseudomonas tends to occur on the wards rather than prior to admission or on an outpatient basis and that infected burns or wounds were the major sources of pseudomonas on the ward.¹⁷

Markley and co-workers¹⁸ during the course of study of burns in Peru encountered a high incidence of fatal septicemia due to *Ps. aeruginosa* clinically manifested by cutaneous lesions which generally preceded death by from 1 to 12 days. The cutaneous lesions involving burn-free areas were of two types. The first and more common of the two was a vesicle which became necrotic and was followed by the appearance of many similar lesions over the body. This type was noted in 72 per cent of children with cutaneous lesions. Generally death occurred from 24 to 48 hours following the appearance of the first vesicle. The second type of lesion was nodular and subcutaneous occurring in 26 per cent of patients with cutaneous lesions. Generally it was followed by death in from 2 to 12 days. The burns at this stage were covered by bluish-green pus or by a black crusted eschar. *Ps. aeruginosa* could be cultured from such areas. An unusual feature of this study was the very high incidence of pseudomonas septicemia in this hospital (29 of 172 burned children developed characteristic cutaneous lesions and of the 25 who were cultured 22 had septicemia due to *Ps. aeruginosa*). The incidence of septicemia in adults was less. No effective therapy was found although antibiotics including polymyxin were administered in the usual dosages.

MENINGITIS

Meningitis due to *Ps. aeruginosa* is uncommon. Neal^{2, 3} in 1935 reviewed 3178 cases of meningitis occurring in New York between

1910 and 1921 she found only 1 attributed to pseudomonas. Tripoli in 1936⁴¹ at Charity Hospital New Orleans reviewed 468 cases of bacterial meningitis from 1925 to 1931. Of the 111 that were due to pseudomonas and 3 were fatal. Barron¹⁶ in 1918 reviewed the literature and found 39 cases of meningitis in infants under 3 months of age. Of 19 reported in the newborn only 1 of them was caused by pseudomonas. Pastor and co-workers found only one meningeal infection from pseudomonas at the Philadelphia General Hospital between 1939 and 1949. More recently Smith collected a series of 409 patients with purulent meningitis at the Children

TABLE 2—Cumulative Data on Recorded Cases of *Pseudomonas* Meningitis

Author and date	Total		Primary		Secondary		Unknown
	No.	Mortality (per cent)	No.	Mortality (per cent)	No.	Mortality (per cent)	
■ an 1936	39	67	17	47	18	83	4
Kernan 1943	55	■	29	45	21	85	6
Stanley 1947	71	68	41	55	30	86	0
Forkner 1957	200	46	144	39	14	66	12

Data through 1955

Hospital in Los Angeles. Bacteria were isolated from 316 cases and only 5 of these were pseudomonas. Of the 5 patients 3 died.³⁰⁴ Nevertheless pseudomonas is possibly the most common cause of bacterial meningitis following lumbar puncture.

Ehlers in 1890 first reported meningitis due to *Ps. aeruginosa* however the cerebrospinal fluid was not cultured.¹¹³ Kossell⁴⁸ in 1893 described the first proved case—an infant whose source of infection was otitis media and from whose purulent heart blood pseudomonas was recovered in pure culture after death. In 1936 Evans¹³ reviewed the literature and collected 39 cases of which 29 were fatal (see TABLE 2). She considered 18 of her cases to be secondary to generalized infection and reported a mortality of 83 per cent. In 1943 Kerman et al.³⁷ assembled 55 cases from the literature and added one of their own which had occurred following pneumoencephalography. A wash bottle used in the procedure was

found to be the source of contamination. Of the 56 cases 21 were secondary to septicemia with a mortality of 85 per cent. The overall mortality from pseudomonas meningitis found by Stanley in 1917 in a review of 71 cases was 63 per cent. Of 41 primary cases the mortality was 55 per cent. Of 30 secondary cases the mortality was 86 per cent. The increasing number of reported cases (primary and secondary) is illustrated in FIGURE 7.

PSEUDOMONAS MENINGITIS

Cumulative Bar Graph of Reported Cases Through 1955

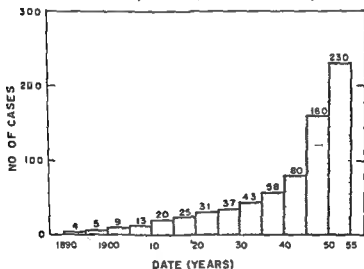


FIG 7—The graph illustrates the increasing number of reported cases of meningitis due to *Pseudomonas aeruginosa* during the last decade.

Reported cases of pseudomonas meningitis have usually been classified as either *primary* or *secondary* in origin. Unfortunately the meaning of these terms has been subject to individual interpretation so that statistical evaluation of cumulative series becomes very difficult. Primary is here defined to mean direct introduction of the bacteria into the central nervous system; secondary shall refer to hematogenous meningitis. Situations involving possible

direct extension of infection such as otitis media³⁹ or mastoiditis³⁹ with subsequent meningitis have been classified according to the clinical features of the case in question.

Schlagenhauser³⁷³ is usually credited with describing the first case of primary pseudomonas meningitis. In 1911 he reported 5 cases developing after spinal anesthesia. The source of contamination was a saline solution. Three of the patients died. Chauffard and Laroche³⁷ in 1917 reported a case following the intrathecal administration of tetanus antitoxin. Other cases have been reported following wound of the head^{1, 41, 50} spinal wounds⁴; infected spina bifida¹⁰⁰ pneumoencephalography^{9, 3} myelography with Pantoque⁶⁶ laminectomy[†] burr holes⁶ radical mastoidectomy³⁷ meningeal ureteral anastomosis for hydrocephalus³⁴³ excision or rupture of meningomyelocele^{33, 36} and exploration for brain tumor⁴¹⁸. The most common preceding event however is lumbar puncture as a diagnostic^{1, 3, 4, 5} anesthetic^{3, 3} or therapeutic^{6, 103} procedure. A chronologic listing of reported primary cases is available in TABLE 3.

TABLE 3—Primary Meningitis

Authors	Year	Age Group	(cases)	Outcome		Remarks
				Died	Recovered	
Schlagenhauser ³⁷³	1911	A	5	3	2	Spinal anesthesia (contaminated saline)
Chauffard and Laroche ³⁷	1917	A	1		1	IT† tetanus antitoxin following football injury
Abadie and Laroche	1918	A	1		1	Head wound. Therapy given serum injected IT

Patients 15 years and over are listed as adults; below 15 years children; and 1 year and under infants.

† Intrathecal

‡ Lumbar puncture

§ Intramuscular

¶ Intravenous

* Streptokinase; † Streptodornase

TABLE 3—*Continued*

Authors	Year	Age Group	Outcome			Remarks
			Cases	Died	Recovered	
Sonnenchein ¹⁰	1923	A	1	1		LP+
Shneider ¹¹	1924	A	1		1	Spinal anesthesia used; yargochryme and araffin
Levy and Cohen	1925	A	1		1	LP IT: activated autogenous blood serum spinal drainage
Vill et al.	1928	A	1		1	Spinal gunshot wound. Therapy autogenous vaccine
Vahant al	1931	A	1		1	? LP or septemia from tooth. Ill
Ghon ¹⁶⁰	1932	I	1	1		Infected pin abscess
Shewbury	1933	A	1		1	Spinal anesthesia. Therapy repeated spinal drainage
Bhatnagar	1934	A	1	1		Spinal anesthesia
Enfield	1936	A	3	2	1	LP
Ibrahim	1937		1		1	LP
Berg	1938		1		1	LP IT: activated autogenous blood serum
Iwasaki and Motono	1939		1			Pneumoencephalography
Wise and Miller	1939		11	2	4	LP (contaminated in recurrent manometer). Therapy: Sulfa and repeated spinal drainage
Kaman et al. ³⁷	1943	C	1	1		Pneumoencephalography (w/ bottle contaminated). Therapy: Sulfa
Bitterli and Minner	1944	A	11	9	2	Petrified head wound (2 from contaminated pencil). Therapy: Penicillin and sulfa
Enfield	1944	A	2	2		Spinal anesthesia (? head wound) contaminated until wat

TABLE 3—Continued

Authors	Year	Age Group	Cases	Outcome		Remarks
				Died	Recovered	
Kremer ⁵⁴	1945	A	4	1	3	2 spinal anesthesia 2 contaminated penicillin
Decourt et al ⁵⁵	1945	A	1		1	Spinal anesthesia Therapy Sulfadiazine
Pulaski and Mathews ⁵⁴⁹	1946	A	1		1	Stem 1 m & 1 v & 1 t
Cairns et al ⁵⁶	1946	A	3	3		Brain abscess from gun bot wounds—Therapy Stem 1 t and in ventricle
Harris et al ¹⁹³	1946	2A	4	1	1	Contaminated penicillin used to treat meningococcal meningitis Therapy Penicillin sulfa drains
		2I		1	1	
Cawthorne ⁶	1946		2			Spinal anesthesia
Davidson ⁹¹	1947	A	2	1	1	Spinal anesthesia Therapy Sulfa
Merwarth et al ³⁰⁷	1947	A	1		1	Spinal anesthesia Therapy Penicillin sulfa
Medicolegal ^{303 304}	1947	A	4	3	1	Spinal anesthesia
Paine et al ³³⁶	1947	C			1	1 LI 2 spinal surgery
		I			1	3 erosion of meningocele
		I		1		Therapy Penicillin sulfa streptomycin
Vuylsteke ⁸	1947	A	4	3	1	Spinal anesthesia Therapy Sulfa
Keefler and Hewitt ³³	1948		9			7 related to LP 2 from cervical meningocele
Lewin and Vollum ⁷⁷	1948	A	2		2	Head wound Therapy Sulfa and streptomycin
Lewin ⁶	1948	A	3	3		Head wounds
Weinstein ⁴⁴¹	1948	A	3		3	Spinal anesthesia Therapy Sulfa penicillin and streptomycin

TABLE 3—Continued

Authors	Year	Age Group	Case	Outcome		Remarks
				Cured	Reverted	
Stoenfack	1919		3			Infected head wound. Therapy at lymph node.
Rafke and Cuningham ¹	1919	C	1		1	Therapy (penicillin, lfa and streptomycin)
Germer and Kapp ¹⁰	1919	A	1	1		LP. Therapy streptomycin
Tillett ⁵	1919	A	1		1	Head wound—7 month cure—finally cured with SKSD
Eugen ³	1919	A	1	1		Spinal neuritis. Therapy penicillin and lfa
Netter et al. ¹⁰	1920	C	1		1	Laminectomy. Therapy Sulf and chloramphenicol
Emmes et al. ¹¹⁷	1920	A	1		1	Therapy intraspinal penicillin and streptomycin—relapse—repeated with o.lulfa (no focus)
Hayes and Yow ¹¹⁸	1920	A	1		1	Spinal neuritis. Appendectomy, polymyositis and lfa
Debre et al. ¹⁰³	1920	I	3	3		1 Ventricular puncture for hydrocephalus. 2 Antrotomy for otitis. Therapy streptomycin and penicillin
Sellmon et al. ⁶	1921	A	1		1	Spinal neuritis—6 relapse—Therapy intracranial streptomycin
Reitter ¹¹⁹	1921	A	1		1	Spinal neuritis. Therapy Sulf
Pedell and Paley ²	1921	A	1		1	Thyroidic LP. Therapy Sulf and streptomycin
Busgaard Brygoo ³	1921	I	1	1		Probably LP (was being treated for pneumococcal meningitis)

TABLE 3—Continued

Authors	Year	Age Group	Cases	Outcome		Remarks
				Died	Recovered	
De bailllets ¹¹	1911	A	1		1	Spinal anesthesia Therapy streptomycin
Laster et al ³³⁷	1951	2A	2		2	Spinal anesthesia Therapy 1t streptomycin
Jawetz ⁶	1952	C	2		2	1 Following burr hole 2 Residual hydrocephalus Therapy polymyxin 1t
Ginsberg and Hyman ¹	1952	A	1		1	Following radical mastoidectomy — streptomycin and chlortetracycline
Kreitner ³	1952	A	1		1	Spinal anesthesia Therapy Sulfa and streptomycin—4 relapses
Schmeisser ^{3, 4}	1952	C	3	1	2	Following diagnostic LPs chloramphenicol 1t and po
Dukowski et al ³³	1952	I	1		1	Following operation on meningocele Therapy neomycin 1m
Knight et al ⁴	1952	A	1		1	Following laminectomy Therapy SK-SD and neomycin 1m and 1t
Troen and Dicaprio ^{4, 8}	1952	A	1		1	Spinal anesthesia Therapy Oxytetracycline
Yow ³⁰	1952		3			No detail
Douha et al ¹⁰⁵	1952	A C I	3	3		Operations for meningocele and hydrocephalus
Cutler and Cutler ⁸⁵	1953	2A	2		2	Spinal anesthesia Therapy Chloramphenicol and oxytetracycline in one and streptomycin in the other
Reitter ³	1953	A	1		1	Spinal anesthesia for hysterectomy

TABLE 3—*Continue d*

Author	Year	Age	Cases	Outcome		Remarks
				Died	Recovered	
Monnet and Lautermilch ¹	1953		1			D diagnostic and therapeutic LP
Piette ^{2,3}	1953	I	1	1		Following meningoureteral anastomosis for hydrocephalus Therapy polymyxin—3 relapses
Smith C E C ⁴	1953	A	1		1	Following LP for skull fracture Therapy Chloramphenicol
Fell ⁵	1954	C	1		1	Following exploration for ependymoma Therapy polymyxin L
Dahl and Hamburger ⁶	1954	A	5	3	2	Following CNS procedures (3 spinal anesthesias 1 menocle 1 spinal treatment) Therapy polymyxin D
Loell Smith ⁷	1954	C	1		1	Following compound fracture of femur for LP Therapy Polymyxin B 1st
Blumg	1954	I	1	1		Following rupture of mylo-cystocele
Mabille et al. ⁸	1955	A	1	1		1 month after bullet head injury Therapy polymyxin B 1st and 2nd
Frey Schmidt ⁹	1955	A	1		1	Symptomatic therapy
Egertson and Olhagen	1955	A	1		1	Symptomatic therapy Therapy oxytetracycline and polymyxin B 1st and 2nd
Boyd et al. ¹⁰	1955	A	1	1		LP (open meningoencephalogram) Therapy streptomycin and polymyxin
Stojic and Vojvodic	1955		1			

Meningeal infection in secondary cases is the result of hematogenous spread from a focus elsewhere in the body. This may be from localized abscesses,⁶ stomatitis,²⁴⁰ enteritis,⁶⁰ or following ureteral instrumentation.⁴¹⁶ The pathway in infants is often via the umbilicus. Meningitis may occur following *in utero* infection³⁴¹ or circumcision. Reported cases of secondary pseudomonas meningitis are chronologically listed in TABLE 4.

TABLE 4—Secondary Meningitis

Authors	Year	Age Group	Cases	Outcome		Remarks
				Died	Recovered	
Fidler ¹¹³	1890	C C	2	1	1	Both had typhoid like septi- cemia (brother and sister). Spinal fluid not cultured.
Koel ¹¹⁴	1894	I	1	1		Otitis media (pure culture of <i>Pseudomonas</i> from pia and heart blood).
Pesina and Honk ²⁴²	1894	A	1	1		Primary site unknown.
Councilman et al ⁶¹	1898		1			Mixed with <i>Staphylococcus aureus</i> .
Perkins ²⁴⁰	1901	A	1	1		Abortion followed by septi- cemia (<i>Pseudomonas</i> in CSF* and liver).
Berka ²	1903	A	1	1		? Pneumonia. Pure cultures from purulent meningeal foci.
Horder ¹¹	1904	A	1	1		Chronic otitis media.
Rolly ²⁴³	1906	A	1	1		Abortion followed by septi- cemia (mitral valve in- volved).
Hubener ²¹⁵	1907	A	1	1		Pelvic abscess opened—led to septicemia and meningit.
Benfey	1907	I	1	1		Infection of umbilicus.
Laiffoul et al ²⁹	1910		1	1		Typhoid like septicemia.

Cerebrospinal fluid

TABLE 4—*Continued*

Authors	Year	Age Group	Outcome			Remarks
			Cured	Died	Recovered	
Finkel	1912	A	1	1		Septicemia—no obvious focus
Gaethlen	1914		1	1		Tuberculous meningitis
Finkel	1917	I	1	1		Cholera toxinemia
Caelli	1919	I	1	1		Enteritis septicaemia
Dudley	1922	C	1	1		Septicemia (femoral abscess)
Neal	1924	C	1			
Klew and Koch	1924	C	1		1	Stomatitis
Charney	1926	I	3	3		Probably umbilical—Pseudomonas in meninges and pericardium
Gauhaud and Pineda	1928	I	1	1		Infection of umbilicus (from amniotic fluid)—(hydrocephalus)
Leidham	1930	A	1	1		No obvious focus
Baumter	1931	A	1		1	No obvious focus
Dei	1933	C	1	1		Septicemia otitis media
Meyer and Pehlin	1935		1		1	Ophthalmic infection in lid
Neh	1936	C	1	1		Mastoiditis
Ritter and Bley	1937	A	1		1	Tuberculous empyema with secondary fistula
Slutsky and Mithin	1939	A	1	1		Septicemia with focus in right kidney—treated with streptomycin
All	1941	I	1	1		Infection of umbilicus (mother had severe Pseudomonas enteritis)
Krueger and Huft	1941	I	1	1		Probably umbilical

Meningeal infection in secondary cases is the result of hematogenous spread from a focus elsewhere in the body. This may be from localized abscesses¹¹ stomatitis²⁴⁰ enteritis⁶⁰ or following ureteral instrumentation.⁴¹⁶ The pathway in infants is often via the umbilicus. Meningitis may occur following *in utero* infection³⁴⁰ or circumcision. Reported cases of secondary pseudomonas meningitis are chronologically listed in TABLE 4.

TABLE 4—Secondary Meningitis

Authors	Year	Age Group	Cases	Outcome		Remarks
				Died	Recovered	
Ehler ¹¹⁵	1890	C C	2	1	1	Both had typhoid like picture (brother and sister). Spinal fluid not cultured.
Kossei ²⁴⁸	1894	I	1	1		Otitis media (pure culture of <i>Pseudomonas</i> from pia and heart blood).
Pesina and Honl ³⁴¹	1894	A	1	1		Primary site unknown.
Councilman et al. ⁸	1898		1			Mixed with <i>Staphylococcus aureus</i> .
Perkins ³⁴⁰	1901	A	1	1		Abortion followed by septicemia (<i>Pseudomonas</i> in CSF and liver).
Berk ²⁵	1903	A	1	1		? Pneumonia. Pure cultures from purulent meningeal foci.
Horder ²¹¹	1904	A	1	1		Chronic otitis media.
Rolly ³⁰³	1906	A	1	1		Abortion followed by septicemia (mitral valve involved).
Hubener ¹³	1907	A	1	1		Pelvic abscess opened—led to septicemia and meningitis.
Bensley	1907	I	1	1		Infection of umbilicus.
Lagniffoul et al. ²⁹	1910		1	1		Typhoid like septicemia.

* Cerebro spinal fluid

TABLE 4—*Continued*

Authors	Year	Age (month)	Cases	Outcome		Remarks
				Died	Recovered	
Fraenkel ⁴⁴	1917	A	1	1		Septicemia—no obvious focus
Caethgen	1918		1	1		Tuberculosis meningitis
Fraenkel ^{44b}	1917	I	1	1		Chronic otitis media
Canalis	1919	I	1	1		Etiology septicemia
Doddens ⁴⁵	1922	C	1	1		Septicemia (from middle ear)
Neal	1924	C	1			
Klewas and Krich	1924	C	1		1	Stomach
Chern ⁴⁶	1927	I	3	3		Probably umbilical— <i>Escherichia coli</i> meningitis and peritonitis
Gauß and Pridmore ⁴⁷	1928	I	1	1		Infection of umbilicus (from amniotic fluid)—(hydrocephalus)
Leidholm ⁴⁸	1930	A	1	1		No obvious focus
Baumgartner	1931	A	1		1	No obvious focus
Beri	1933	C	1	1		Septicemia of the media
Myer and Relling	1933		1		1	Otitis externa from foreign body
Nichols	1936	C	1	1		Meningitis
Rosenfeld and Fejsey	1937	A	1		1	Tuberculous empyema with secondary infection
Slutsky and Mail	1939	A	1	1		Septicemia with focus in right kidney—treated with sulfamerazine
Allen	1941	I	1	1		Infection of umbilicus (mother had severe <i>Perfringens</i> enteritis)
Krawiec and Hunter	1941	I	1	1		Probably umbilical

TABLE 4—Continued

Authors	Year	Age Group	Cases	Outcome		Remarks
				Died	Recovered	
Moragues and Anderson ¹⁹	1943	A	1	1		Infection of urinary tract
Aulnik	1946	I	1	1		Circumcision. Treated with ultra penicillin and spinal drainage
Stanley ⁴³⁴	194	C	1	1		Septicemia treated with streptomycin
Keefer and Hewitt ³³	1948		2			Secondary to septicemia
Schaffer and Oppenheimer ³⁸	1948	I	2	2		Septicemia from appendix
Hirzfeld et al ⁶	1948	I	2	2		Therapy L.P. Therapy sul fathiazol
Viklicky ⁴⁰	1948		1	1		Hepatic abscesses or cysts
Debre and Mozziconacci ⁹⁴	1949	I	4	3	1	Septicemia from intestinal tract—Therapy streptomycin and it
Appelbaum et al	1949		4	2	2	Introduced during it penicillin for pneumococcal meningitis
Zimmermann ⁴⁶	1949		4	4		2 love gastro intestinal and 2 rhinopharyngitis—Therapy penicillin sulfa and streptomycin
Glanzmann ¹⁴	1950	C	1		1	Unknown focus. Therapy it penicillin and streptomycin
Lodenkamper and Schiersmann ⁸	1950	A	3		3	2 after encephalography 1 after suboccipital puncture. Treated with autovaccine sulfonamides spinal tap. Blood transfusion 1 had convalescent serum it

TABLE 4—Continued

Authors	Year	Age Group	Cases	Outcome		Remarks
				Died	Recovered	
L Jones	1950	A	1		1	Followed abortion (LP not excluded) The apy trepto mycin and sulf
Fa eka and N kod mu z	1950	C	1		1	Focal intestinal tract Therapy penicillin streptomycin
Co co et al	1950	I	1		1	Septicemia (GI tract) Therapy penicillin streptomycin
Tomlinson	1951	A	1		1	Septicemia following enteric infection — Therapy polymyxin B
L u i d Br v o	1951	I	1		1	Umbilicus
C n ber and Hyman	1952					
Weishe	1952	C	1		1	Bilateral mastitis treated with streptomycin after penicillin failed
And et al	1952	I	1	1		Hematogenous from abscess
D uha tal	1952	I	1	1		Septicemia (? from thigh abscess)
L nzan o and Mold	1953	C	1		1	Lapotomy for appendectomy ? intestinal tract Therapy polymyxin B (? LP)
Pefer et al	1953	C	1		1	Occurred 1 month after perforated appendix Therapy oxytetracycline and streptomycin
Ma a id D t t n	1953	I	1		1	? Hematogenous (LP not excluded) Therapy polymyxin B

TABLE 4—Continued

Authors	Year	Age Group	Outcome			Remarks
			Cases	Died	Recovered	
Moraes and Anderson ¹⁸	1943	A	1	1		Infection of urinary tract
Azulnik ²	1946	I	1	1		Circumcision. Treated with sulfa, penicillin and spinal drains ⁶
Stanley ^{4, 4}	194	I	1	1		Septicemia treated with streptomycin
Keefer and Hewitt ³³	1948		2			Secondary in septicemia
Schaffer and Oppenheimer ^{3, 3}	1948	I	2	2		Septicemia from appendix
Hirzfeld et al ²⁰⁴	1948	I	2	2		Therapy LI. Therapy Sul fathiazol
Viklicky ^{4, 6}	1948		1	1		Hepatic abscess or cystitis
Debre and Mozziconacci ⁴	1949	I	4	3	1	Septicemia from intestinal tract—Therapy streptomycin and it
Appelbaum et al ⁶	1949		4	2	2	Introduced during it penicillin for pneumococcal meningitis
Zimmermann ⁴⁶	1949		4	4		2 lower in trinitis and 2 rhinopharyngitis—Therapy penicillin sulfa and streptomycin
Glanzmann ⁷	1950	C	1		1	Unknown focus. Therapy it penicillin and streptomycin
Lodenkamper and Schiermann ⁵	1950	A	3		3	2 after encephalography. 1 after suboccipital puncture. Treated with autovaccine, sulfonamides, spinal tap. Blood transfusion. 1 had convalescent rum it

Information derived from sensitivity studies on bacterial cultures is often of critical importance in prescribing therapy Levaditi³⁵ reported the identification of *Ps. aeruginosa* cultures by using ultraviolet light to demonstrate the fluorescent greenish yellow pigment This technic has been used in the diagnostic evaluation of spinal fluid³⁸

The characteristic relapsing course of pseudomonas meningitis may be explained by the anatomic changes in the central nervous system Fibrin may be deposited in the subarachnoid space the infected cerebrospinal fluid may be loculated by adhesions These collections resistant to therapy may remain for long periods of time before releasing their contents into the circulating spinal fluid Kremer³⁴ report that so long as the condition is confined mainly to the spinal canal the arachnoiditis is not likely to cause serious complication however if infection involves the brain adhesion may obstruct the flow of cerebrospinal fluid causing hydrocephalus He attributed rigidity of the back to irritation of spinal roots from fibrinopurulent cuffing of the nerve roots

At necropsy the brain in pseudomonas meningitis is covered to some extent by a greenish yellow exudate Typical histologic findings of the meninges are illustrated in FIGURE 10

Prior to the discovery of sulfonamides pseudomonas meningitis was treated by spinal drainage³⁶ or by autogenous vaccine administered intrathecally³⁷ In general the results of therapy were poor however some patients recovered³⁸⁻⁴⁰ Penicillin and sulfonamides had no apparent effect on the mortality statistics Harris and co-workers¹⁹³ in 1946 reviewed the results of the use of sulfonamides and penicillin in this disease and found that of 21 patients treated with these drugs 15 (72 per cent) died For several years case reports of many writers attest to the popularity of streptomycin⁴¹

19 27 311 337 403 431 Weinlein and Perrin summarized four recoveries among nine patients treated with streptomycin⁴¹ At that time although certain disadvantages were apparent a combination of sulfonamides and streptomycin was considered the therapy of choice Intrathecal injection of streptomycin was frequently associated with an increased number of cells in the cerebrospinal fluid and exces-

TABLE 4—Continued

Authors	Year	Age Group	Outcome			Remarks
			Cases	Died	Recovered	
Heinecker ¹⁰⁹	1953	C	1		1	Unknown focus—treated with chlortetracycline and frequent L.P.s—air introduced
Wideman ⁴⁴⁵	1953	I	1	1		Upper respiratory infection—died 12 hours after admission
Chamber ¹¹	1953	I	1	1		Intestinal tract (? L.P.) Therapy chloramphenicol and penicillin
Jansen ²⁵	1954	I	1	1		Therapy chlortetracycline polymyxin B and streptomycin and it
Hoffman ²⁰⁸	1954	I	1	1		? Congenital infection
Smith R T ³⁹⁵	1955	I	1		1	Septicemia oxytetracycline and chloramphenicol
Jones R F M	1955	A	1		1	Chronic otitis and suppurative otitis media Therapy polymyxin B it and it

Clinical signs of pseudomonas meningitis usually appear within 24 to 48 hours after seeding but may be delayed. The onset is rapid with nuchal rigidity and a high spiking fever. Polymorphonuclear leukocytosis is common in the spinal fluid. Characteristically the spinal fluid is cloudy and contains increased albumin and fibrin and decreased sugar. Commonly few or no bacteria are seen on smears of the spinal fluid. The disease may either terminate rapidly with cure or result in rapid death of the patient. Frequently however a chronic indolent apparently low grade infection will supervene which is resistant to many or all antibiotic agent. Apparent cure is often followed anywhere from days to months by relapse which may recur many times in the absence of appropriate therapy.

sively large individual doses were known to have caused serious reactions^{36, 37a}

Tillet⁴¹ in 1919 described the successful use of enzymes in the treatment of meningitis due to *Pseudomonas*. SK SD (15 000 units streptokinase and 3750 units of streptodornase) was injected intrathecally at two day interval. In one patient meningitis which had been refractory to treatment with sulfonamide, chlorotetracycline, chloramphenicol and streptomycin for seven months responded quickly. The issue is confused however since intrathecal and intramuscular neomycin was given concurrently. Knight et al.⁴² in 1952 also reported the successful use of intrathecal SK SD in conjunction with neomycin in a case of *Pseudomonas* meningitis which had followed laminectomy.

Occasional favorable reports followed the use of chlorotetracycline⁴³, oxytetracycline⁴⁴, combined oxytetracycline and chloramphenicol⁴⁵ and chloramphenicol alone.⁴⁶ A combination of chlorotetracycline and streptomycin was used successfully³⁷ in one case.

A number of factors may in part be responsible for the increase in number of reported cases during the last few years (FIGURE 7). Among these are the advent of antibiotics with the tendency to report only successful therapy, the increasing number of medical authors and journals, and an increasing awareness of and interest in the disease. The more frequent use of lumbar puncture for spinal anesthesia as well for other diagnostic and therapeutic procedures is not the only factor since the incidence of secondary as well as primary meningitis has increased.

Through the year 1955 at least 230 cases of *Pseudomonas* meningitis have been referred to in the literature, about 60 per cent of these are considered primary. The remaining cases are considered secondary to a septic focus elsewhere in the body. Of the 111 primary cases 39 per cent were fatal, of the 74 secondary cases 66 per cent were fatal. The overall mortality rate is 46 per cent. This information is illustrated in TABLE 2. Although the incidence of meningitis would appear to be increasing the mortality for both primary and secondary cases is decreasing.

At the Clinical Center 6 cases of meningitis secondary to *Pseu*

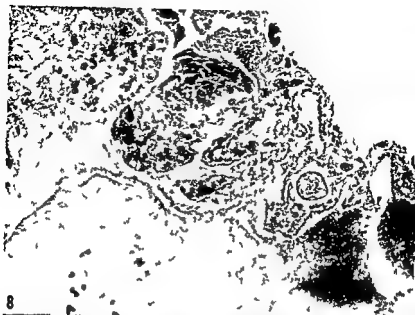


FIG. 8—(above) Hemorrhages and thrombi. *Pseudomonas meningitis*.

FIG. 9—(below) Pulmonary abscess. Possible portal of entry: Bronchiole; chronic atherothrombotic athero-calcification; large pulmonary vessel.

Pneumothorax suddenly occurred and *empyema* developed. On drainage of the pleural space *pseudomonas* was cultured from the exudate. Sterility of the lesions and clinical cure followed repeated blood transfusions and local and intramuscular therapy with penicillin and streptomycin. In a series of 37 patients with *pseudomonas* infection, Yow⁴⁰ listed 5 with parenchymal pulmonary infection and 1 other with *empyema*. All these cases developed during or following treatment with antibiotics. Firket and Douha¹⁵¹ described 1 adult with *pseudomonas* infection in the pleural cavity. In only one of the cases was there no previous history of instrumentation through the pleura. Other cases have been reported.^{73 109 145 155}

Bronchopneumonia has frequently been reported.^{1 9 109 111 15}
 11 43 5 93 113 210 301 306 41 425. A case from our own files is that of H.K. with chronic lymphocytic leukemia who had received irradiation and who was being treated with adrenal cortical steroid compounds. She developed a chronic productive cough accompanied by fever and chills. *Ps. aeruginosa* was cultured from the nose, throat, sputum and urine. On x-ray an infiltrate was seen in the right upper lobe. For two months her cough persisted as did the *pseudomonas* in her sputum. She received intensive treatment with penicillin, streptomycin, sulfonamides and polymyxin B. She developed anasarca and pleural effusions, became disoriented and died. The necropsy findings included septic thrombosis of a pulmonary artery and vein in the lower lobe of the left lung, septic thrombi and emboli and infarcts in the brain, thyroid gland, heart, lungs and kidneys (FIGURE 9).

There have been several reports of fibrocystic disease of the pancreas associated with *pseudomonas* infection of the lung. Garrard et al.¹⁵⁶ observed 4 consecutive patients with pancreatic fibrosis in whom *pseudomonas* was the predominant organism demonstrable in the respiratory tract. All had received prolonged antimicrobial therapy. One had suppurative bronchitis and bronchiectasis with multiple pulmonary abscesses from which *pseudomonas* was grown in pure culture. Another had suppurative bronchitis with purulent viscid secretions forming a cast of the bronchial tree from this *pseudomonas* was obtained in pure culture. A third had acute and

domonas septicemia were diagnosed over a three year period from 1954 to 1957. All of the patients had leukemia. Definitive diagnoses in most cases were made only at autopsy because of short survival times and overwhelming septicemia.

RESPIRATORY INFECTION

Pulmonary lesions like cutaneous or meningeal lesions may be primary or secondary in origin and the evidence for one or the other is not always conclusive. The respiratory tree seems seldom to be the portal of entry; convincing reports of primary pulmonary infections are not common. Meltzer^{33*} was able to produce broncho pneumonia in dogs by insufflation of suspension of *Ps aeruginosa*. Once established respiratory infections with pseudomonas are often fatal.^{73 100 101 370 371 378 404} Infections in some patients may be prolonged and may respond to various forms of therapy.^{1 87 1 173 8} There is little doubt that the use of antibiotics has been a factor in the establishment of some of these infections.^{3 301 440 480}

Pulmonary abscesses caused by pseudomonas may be single or multiple. Robitzek³⁸¹ in 1946 reported a 5 month old infant with severe paroxysmal cough and fever for two months. He became critically ill with cyanosis and dyspnea. Treatment was instituted with sulfonamides and penicillin. Numerous gram negative bacilli were seen in the sputum. The pneumonia spread to the right upper lobe and the infant died. At autopsy the trachea and bronchi were filled with purulent mucus. Numerous firm gray hemorrhagic patches 1.5 to 3 cm in diameter were in all lobes. In the left upper lobe there was an irregular 5 by 7 cm cavity with a smooth gray membranous lining. This contained gelatinous material from which *Ps aeruginosa* was cultured. The authors considered this infection to have been of primary pulmonary origin.

Pseudomonas empyema and pleuritis have been observed. Clanzmann^{1 4} in 1950 reported a 3 and one half month old infant with rhinopharyngitis and fever. The abdomen became tender and distended and intestinal ception was suspected. A bloody mucous enteritis developed and pseudomonas was cultured from the stool.

old male by Raim in 1935³³ The patient was dyspneic had enlarged tonsil and rapidly developed tridor cyanosis and unconsciousness The epiglottis was large red edematous and contained a central elevated yellowish area which was open and draining Pseudomonas was cultured from this and uneventful recovery followed therapy with furazolidin

GASTROENTERITIS

Lesions of the gastrointestinal tract due to *Ps. aeruginosa* are similar in histologic appearance to those observed in other parts of the body they may arise from within the intestinal tract or by way of the blood stream Experimentally irradiated mice are known to die with overwhelming spontaneous septicemia due to pseudomonas and other gram negative bacteria normally found in their intestines^{31, 390} The feeding of broth cultures of organisms^{1, 9} or of mucin to irradiated mice increases the mortality A similar alteration of host bacteria relationship in man is suggested by the occurrence without evident portals of entry of septicemia due to pseudomonas and other intestinal flora in debilitated patients

There has been much speculation regarding the possible causative role of pseudomonas in epidemic diarrheas of the newborn The organism is found sufficiently often in the stools of asymptomatic persons to make evaluation of this difficult In adults pseudomonas enteritis has been confused with typhoid fever and is more frequently observed in the tropic¹³⁷ Bloody diarrhea⁴⁶⁴ is the common initial and persistent symptom Fever vomiting dehydration skin rashes and jaundice are noted frequently

Epstein and Grossman¹¹⁹ have reviewed the literature to 1933 mentioning the early cases and epidemics of enteric pseudomonas infection^{71, 57, 79, 109, 111, 144, 147, 33, 64, 371, 43, 4} Ensign and Hunter¹¹⁹ in 1946 reported an epidemic of diarrhea in 24 newborn infants in which there were nine deaths Of these infants 18 contracted the disease in a nursery All 9 infants who were studied bacteriologically had pseudomonas in their stools Symptoms in order of frequency were diarrhea vomiting dehydration cyanosis collapse pain and fever Treatment consisted of transfusions par

chronic bronchitis bronchiectasis and bronchopneumonia Other cases of this nature have been reported^{80 108 151 15}

Infection with pseudomonas may be manifest as bronchitis O'Brien¹⁵⁰ in 1950 described a 10 week old boy admitted with a productive cough his illness was diagnosed as pseudomonas tracheitis and bronchitis He died in eight weeks in spite of treatment with sulfonamides and penicillin At autopsy bronchitis and pneumonia were found *Ps aeruginosa* was obtained in pure culture One year later a sister of the first patient developed pertussis at 6 weeks of age The sputum was positive for *Ps aeruginosa* Treatment with sulfonamides penicillin streptomycin and polymyxin A was unsuccessful and she died at the age of 9 and one half months Other patients with bronchitis due to *Ps aeruginosa* have been reported^{7 143 147 315 383} Pertussis-like syndromes also have been noted^{100 361}

Infection of the lungs due to *Ps aeruginosa* may give rise to asthma-like symptoms which are a result of increased secretions edema and bronchospasm Jawetz¹ reported a 51 year old patient with a history of asthma who had received large doses of antibiotics A Caldwell-Luc procedure had been done for relief of pseudomonas sinusitis The patient had purulent sputum postnasal drainage wheezes and rales in the lungs Cultures of the sinuses and sputum yielded predominantly *Ps aeruginosa* After a week of treatment with intramuscular polymyxin there was improvement in asthmatic symptoms sputum cultures became sterile Fein¹ reported a 7 year old girl who over a period of three months had received penicillin chlortetracycline oxytetracycline and streptomycin for bronchial asthma Because of continued wheezing and croupy cough the patient was admitted for bronchocopy Pseudomonas was seen on smears of the bronchial aspirate and was grown in pure culture from the same specimen culture of the sputum had been negative Subsequent treatment with chloramphenicol and polymyxin B resulted in complete relief from asthma

Ulcers of the larynx trachea or other upper respiratory structures due to *Ps aeruginosa* have been reported^{7 46 383} Acute epiglottic abscess due to pseudomonas was reported in a 12 year

enteral fluids, penicillin, sulfonamides, and methylene blue. The source of contamination was an infected rag which had been dripping into pasteurized milk. At a dairy, Schaffer and Oppenheimer³⁰ in 1944 reported infants with severe enteritis due to pseudomonas. One patient had gangrenous appendicitis and another



12

FIG. 12.—Appendix and cecum. Acute appendicitis due to pseudomonas.

multiple perforations of the intestine. Other complications included ileus, dehydration, acidosis, leukopenia, and hypoplasia of the bone marrow. Only a single infant treated with streptomycin survived. Walker⁴²³ in 1952 reported 3 infants with diarrhea, vomiting, and fever, all of whom had pseudomonas cultured from their stools. Clinical improvement and negative stool cultures followed treatment with polymyxin B in 2 cases. The third patient died with septicemia, cyanosis, and jaundice developed 12 hours after polymyxin was started. Post mortem cultures of the stools were negative for pseudomonas.



10



11

FIG 10—(above) Enteric ulcerations and hemorrhagic colitis

FIG 11—(below) Enteric ulcerations. Mixed *Candida albicans* and *Pseudomonas aeruginosa* infection

pital dry. At autopsy in the ileum, cecum and colon were many small ulcers characterized by rolled borders, undermined edges and little inflammatory reaction. Gram negative rod shaped bacteria were found in abundance at the ulcer margins and pure cultures of pseudomonas were obtained from the lesion. The wall of the ileum was greatly thickened, gas bubbles were present between the mucosa and muscular wall. The pathologic diagnosis was pneumatosis cystoides intestinalis. Holgate⁹ in 1954 described a 13 year old female who was hospitalized with fever, diarrhea and abdominal pain. Chloramphenicol was administered. A rose spot, lightly raised rash was noticed shortly before she lapsed into unconsciousness. She was thought to have typhoid fever and died on the sixteenth day. Blood cultures were negative but stool cultures contained a heavy growth of pseudomonas. Mills and Kagan¹⁰ gave oral polymyxin B to ambulatory symptomatic and asymptomatic individuals who were discovered to harbor pseudomonas in the intestinal tract. Other related reports are available.^{31, 6, 74, 83, 104, 139, 1, 157, 14, 88, 311, 4, 5}

The incidence of gastrointestinal diarrhea has been lower in our patients than in several other reported series. However, one patient had extensive ulcerative and hemorrhagic colitis (FIGURE 10), another had gangrenous esophagitis (Mixed *Candida albicans* and *Is aeruginosa* FIGURE 11). A third patient had appendicitis caused by *Ps aeruginosa* (FIGURES 12 and 13).

GENITOURINARY TRACT

Data compiled from several sources^{9, 114, 39} indicate that *Ps aeruginosa* is responsible for about 5 per cent of urinary tract infections. Under certain conditions (a virulent resistant strain and a debilitated susceptible host) infection may rapidly lead to fatal septicemia. Frequently however as in many cases of primary pseudomonas meningitis, it is the physician who unwittingly introduces the infection by instrumental or operative maneuvers. The catheter chill, a phenomenon frequently noted after minor operative manipulation of the urinary tract, has been associated with the introduc-

Ceppert and co workers¹⁶¹ cited the case of a 1 year old girl who was hospitalized with a history of diarrhea for two months. She had been receiving penicillin for two weeks prior to admission. *Pseudomonas* was the predominant organism cultured from her stools. She was febrile, dehydrated, marasmic and died on the fourth hos-



13

FIG 13—Appendicitis due to *Ps. aeruginosa*

eme 18. She was lethargic but there were no localizing neurologic signs. The subsequent course illustrated in FIGURE 11 *Ps. aeruginosa* and *E. coli* were cultured from the blood and urine. Antibiotics were continued and blood cultures were negative after five days.

Waisbren⁴ studied 29 patients with 31 bacteremias due to gram-negative organisms. 5 were due to *Pseudomonas* and the genitourinary tract was considered the portal of entry in 4 of these. Martin³⁹ in 1954 reported 10 cases of bacteremia due to *Ps. aeruginosa*. In 7 the portal of entry was the genitourinary tract. In 5 of these an operative procedure on the genitourinary tract preceded the bacteremia. Koch⁴² reported 50 cases of bacteremia due to gram-negative bacteria. Over half the cases arose in the urinary tract. The operative procedure most frequently followed by bacteremia was transurethral prostatic resection. Of the 6 *Pseudomonas* bacteremias 5 were preceded by instrumentation. Of the six patients 3 died. Associated findings included cystopyelonephritis, abscess of the kidney and pneumonia. Spittel et al. reported 12 cases of bacteremia due to *Ps. aeruginosa* treated at the Mayo Clinic.⁴⁰ Six of these originated in the genitourinary tract, 5 after cystoscopy and 1 following ureterotomy. In 5 the portal of entry was unknown.

Although ascending infections are usually limited to the urinary bladder, Stanley⁴⁴ reported a paraplegic debilitated 52-year-old female who developed gangrenous cystopyelonephritis and died with *Pseudomonas* septicemia. Similar cases have been described.^{41, 43} Reports of infection of the prostate and epididymis have been published.^{45, 46, 47, 48, 49, 50, 51, 52, 53, 54} Orchitis has been caused by *Pseudomonas*.^{55, 56, 57} Fatal meningitis due to *Ps. aeruginosa* has followed circumcision complicated by infection.

Keefer and Hewitt⁵ in 1948 accumulated reports on 61 cases of acute infection of the urinary tract in which *Ps. aeruginosa* was isolated as a single etiologic agent. The primary clinical diagnoses were perinephritic abscess (2 cases), kidney abscess (1 case), acute cystitis (16 cases), pyonephrosis (2 cases), and acute infection of the urinary tract (28 cases). In 5 cases calculi were present. 6 patients had a cord bladder and 12 patients had obstruction of the lower urinary tract. In 7 per cent bacteremia was present prior

tion into the bloodstream of living bacteria. A small but significant proportion of these infections are caused by *Pseudomonas*.

Of 23 reported cases of pseudomonas septicemia occurring at the Clinical Center¹⁴⁰ the sole survivor was a 54 year old female (E. L.)

PATIENT E. L.
CARCINOMA CERVIX

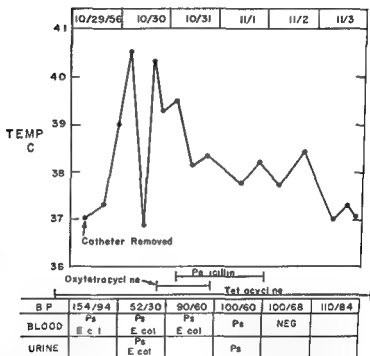


FIG. 14—Febrile reaction to *Pseudomonas* septicemia following injury to lower urinary tract.

who was treated for carcinoma of the cervix by anterior pelvic exenteration and implantation of the ureters into an ileo tomy. Her recovery was uneventful until three weeks after operation when *Ps. aeruginosa* was cultured from the ureter. One month later a ureteral catheter was removed with some bleeding from the ureteral mucosa. There followed in a few hours a sudden shaking chill and fever to 40.5°C. Her blood pressure dropped from normal ranges to 52 mm Hg systolic over 30 mm Hg diastolic. There was some bloody

emic. She was lethargic but there were no localizing neurologic signs. The subsequent course illustrated in FIGURE 14. *Ps. aeruginosa* and *E. coli* were cultured from the blood and urine. Antibiotics were continued and blood cultures were negative after five days.

Walbran⁴ studied 29 patients with 31 bacteremias due to gram-negative organisms. 5 were due to *Pseudomonas* and the genitourinary tract was considered the portal of entry in 4 of the 5. Martin⁵ in 1954 reported 10 cases of bacteremia due to *Ps. aeruginosa*. In 7 the portal of entry was the genitourinary tract. In 5 of the 7 an operative procedure on the genitourinary tract preceded the bacteremia. Koch⁴³ reported 50 cases of bacteremia due to gram-negative bacteria. Over half the cases arose in the urinary tract. The operative procedure most frequently followed by bacteremia was transurethral prostatic resection. Of the 6 *Pseudomonas* bacteremias 5 were preceded by instrumentation. Of the six patients 3 died. Associated findings included cystopyelonephritis, abscess of the kidney, and pneumonia. Spittel et al. reported 12 cases of bacteremia due to *Ps. aeruginosa* treated at the Mayo Clinic.⁴³ Six of these originated in the genitourinary tract, 5 after cystoscopy and 1 following ureterotomy. In 5 the portal of entry was unknown.

Although ascending infections are usually limited to the urinary bladder, Stanley⁴⁴ reported a paraplegic debilitated 52-year-old female who developed gangrenous cystopyelonephritis and died with pseudomonas septicemia. Similar cases have been described.⁴⁵ Reports of infection of the prostate and epididymis have been published.^{1, 133, 41, 371} Orchitis has been caused by *Pseudomonas*.^{1, 371} Fatal meningitis due to *Ps. aeruginosa* has followed circumcision complicated by infection.

Keefer and Hewitt⁴¹ in 1948 accumulated reports on 61 cases of acute infection of the urinary tract in which *Ps. aeruginosa* was isolated as a single etiologic agent. The primary clinical diagnoses were perinephritic abscess (2 cases), kidney abscess (1 case), acute cystitis (16 cases), pyonephrosis (2 cases), and acute infection of the urinary tract (28 cases). In 5 cases calculi were present. 6 patients had a cord bladder and 12 patients had obstruction of the lower urinary tract. In 7 per cent bacteremia was present prior

to treatment Bacteriologic cure with streptomycin was obtained in 30 patients (49 per cent) *Pseudomonas* bacteremia was present in 3 of the 5 fatal cases and uremia was a feature in all fatal cases *Pseudomonas* was associated with *E. coli* (14 cases) *A. aerogenes* (9 cases), and various gram positive organisms (9 cases) *Pseudomonas* was the etiologic agent in 74 chronic urinary tract infections chronic cystitis (8 cases) subacute cystitis (2 cases), hydronephrosis (1 case) chronic pyelonephritis (25 cases), subacute pyelonephritis (11 cases) pyonephrosis (3 cases) chronic infection of the urinary tract (24 cases) Urinary calculi were present in 12 cases Bacteriologic cure was obtained with streptomycin in 31 patient (42 per cent) There was one death *Pseudomonas* was associated with gram negative organisms in 26 cases with gram positive organisms in 6 cases and with combined gram negative and gram positive organisms in 8 cases

Carroll and co workers⁶ using streptomycin treated 39 patients

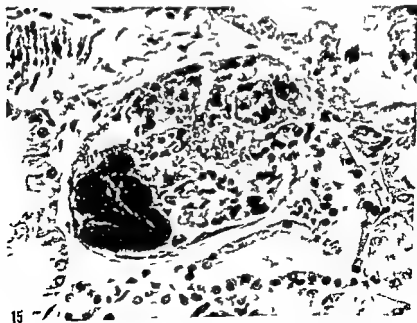


FIG 15—Colony of *Ps. aeruginosa* renal glomerulus Hematoxylin eosin ($\times 400$)

with infections of the urinary tract due to *Ps aeruginosa* and obtained satisfactory results in cases where in vitro testing demonstrated reasonable susceptibility. Systemic toxic symptoms—chills, fever, and frequency and urgency of urination—were common. Ulcers of the bladder were observed, and large pieces of vesical membrane occasionally sloughed into the urine. According to the authors, pseudomonas organisms have the capacity to increase the alkalinity of the urine which may contribute to a sensation of burning on urination and lead to the formation of precipitates and encrustations. Such encrustations may cover the bladder wall and partially or completely block indwelling catheters.

As in the case of epidemic diarrheas, pseudomonas may spread rapidly through a urological ward. Pyrah and co-workers^{31a} described an outbreak in a ward devoted largely to the treatment of prostatic disease. The epidemic was finally terminated by adopting a closed system of drainage of the bladder and by using better technique of sterilization.

Histopathologic lesions of the kidneys have been noted in three of our patients. FIGURE 15 shows a pseudomonas colony residing in a renal glomerulus. This lesion presumably was the consequence of septicemia.

PSEUDOMONAS INFECTIONS ASSOCIATED WITH PREGNANCY

In TABLE 5 are listed chronologically the reported cases of puerperal and/or congenital generalized infections due to *Ps aeruginosa*.

TABLE 5.—A Chronologic Listing of Reported Cases of Puerperal and/or Congenital Pseudomonas Infection

Author ³²	A case of puerperal infection
1889	
Perkin	? case, age 21 and 1 year. The first half infection following septicemia and incomplete abortion and died 1 after 7 weeks. <i>Pseudomonas</i> was cultured from uterine exudates and from perineal fluid.
1901	The second half chills and fever after delivery and died 6 weeks postpartum with purulent endometritis and lungs abscesses. <i>Pseudomonas</i> was cultured from the case.

TABLE 5—*Continued*

Walthard ⁴³⁵ 1904	A 35 year old multipara with chills and fever 3 day postpartum <i>Pseudomonas</i> was cultured from the lochia along with other organisms. The patient recovered.
Rolly ³⁶³ 1906	Following a septic and incomplete abortion <i>Pseudomonas</i> was cultured from the patient's blood and spinal fluid. She died on the 11th day. <i>Pseudomonas</i> was cultured from the heart valves and most of the body organs.
Delmotte ⁹ 1910	An 16 year old primipara was febrile 2 days after spontaneous delivery. <i>Pseudomonas</i> was cultured from the lochia but blood cultures were negative. The patient recovered.
Seifer 1928	A 34 year old multipara with pain, fever and chills following incomplete septic abortion was induced and the product of a 2 month gestation recovered. <i>Pseudomonas</i> was cultured from the blood and placenta. She recovered.
Caucheraud and Pigeau ¹⁶ 1928	The mother had septic endometritis at delivery but recovered in 10 days. 4 days after delivery the infant developed meningitis and hydrocephalus. <i>Pseudomonas</i> was cultured from the ventricular aspirate and the infant died on the 34th day (? contaminated spinal tap).
Allin ⁴ 1941	A 27 year old patient had fever, vomiting and diarrhea during delivery of a premature infant (34 week). <i>Pseudomonas</i> was cultured from the mother's stool. She recovered and was discharged after a 1 month illness. On the 5th day the infant developed red macular areas over the body and died with <i>Pseudomonas</i> meningitis.
Kraus and Hunter ⁵ 1941	The patient had enteritis the day before and chills during delivery. Stools were positive for <i>Pseudomonas</i> . The infant died 20 hours later with cyanosis, dyspnea, leukopenia and a macular rash. Culture of the infant's blood, pleural exudate and brain exudate were positive for <i>Pseudomonas</i> .
Keffer and Hewitt ³³ 1947	No clinical detail. The patient died.
Sobhi and Khairat ³²⁶ 1949	A 28 year old patient at term, the 3rd month of gestation after a 2 day first trimester abortion.

TABLE 5—*Continued*

urine, stool and cervix were positive for *Pseudomonas*. She died 33 days later. Post-mortem cultures from the pericardial fluid and lungs were positive for *Pseudomonas* and *E. coli*.

Hill 1949	A 28 year old primipara was induced in the 7th month of pregnancy because of pre-eclamptic toxemia. She was delivered of a stillborn female and a male who died in 41 hour. <i>Pseudomonas</i> was cultured from the patient's blood, urine and cervix and he died after a 4 month illness with <i>Pseudomonas</i> septicemia.
Nelson and Quinn 1952	A 29 year old primipara had diarrhoea for 1 month prior to abortion at 5 month gestation. She died on the 37th hospital day having had erythema all over her body. <i>Pseudomonas</i> was cultured from the lochia, amniotic fluid, knee lesion, mouth ulcers, tracheal pleural fluid, nasal exudate and feces. The infant appeared normal but died 12 hours after birth with intensely cyanotic discoloration and pleen. <i>Pseudomonas</i> was recovered from the infant's liver, pleen, bone marrow and meninges.
Hoffman 1954	A male twin infant was edematous, dyspneic and cyanotic and died 5 days after birth. <i>Pseudomonas</i> was cultured from the pleural exudate. The infant also had meningitis and myocarditis. The mother was well.
Loftis 1955	The mother had erythema after the 6th month of pregnancy. A full term male infant died on the 4th day with dyspnea, cyanosis and skin macule. <i>Pseudomonas</i> was cultured from the infant's middle ear, liver, gall bladder and pleura.
Stough and Shinner 1956	2 cases. A 38 year old multipara had chill and fever for 7 days and aborted a 3 1/2 lb fetus. Her blood culture was positive for <i>Pseudomonas</i> but she improved and recovered. The fetus was not infected. A 29 year old multipara was delivered of a stillborn male at 36 weeks gestation. She had backache, nausea, vomiting, chill and fever. Her blood and stools were positive for <i>Pseudomonas</i> which was also grown from the blood, lung and pleen of the infant.

TABLE 5—Continued

Walshard ⁴³⁵ 1904	A 35 year old multipara with chills and fever 3 days postpartum <i>Pseudomonas</i> was cultured from the lochia along with other organism. The patient recovered.
Rolly ³⁶³ 1906	Following a septic and incomplete abortion <i>Pseudomonas</i> was cultured from the patient's blood and spinal fluid. She died on the 11th day. <i>Pseudomonas</i> was cultured from the heart valve and most of the body organs.
Delmotte 1910	An 18 year old primipara was febrile 11 days after spontaneous delivery. <i>Pseudomonas</i> was cultured from the lochia but blood cultures were negative. The patient recovered.
Soifer ³⁰ 1928	A 34 year old multipara with pain, fever and chill following incomplete septic abortion was induced and the products of a 2 month gestation recovered. <i>Pseudomonas</i> was cultured from the blood and placenta. She recovered.
Gaucheraud and Pigeaud ¹ 1928	The mother had septic endometritis at delivery but recovered in 10 days. 4 days after delivery the infant developed meningitis and hydrocephalus. <i>Pseudomonas</i> was cultured from the ventricular aspirate and the infant died on the 37th day (? contaminated spinal tap).
Alha ⁴ 1941	A 27 year old patient had fever, vomiting and diarrhea during delivery of a premature infant (34 weeks). <i>Pseudomonas</i> was cultured from the mother's stool. She recovered and was discharged after a 1 month illness. On the 5th day the infant developed red macular areas over the body and died with <i>Pseudomonas</i> meningitis.
Kranz and Hunter 1941	The patient had enteritis the day before and chill during delivery. Stool were positive for <i>Pseudomonas</i> . The infant died 20 hours later with cyanosis, dyspnea, leukopenia and a macular rash. Culture of the infant's blood, pleural exudate and brain exudate were positive for <i>Pseudomonas</i> .
Keefer and Hewitt ³⁵ 1946	No clinical detail. The patient died.
Soliman and Kharrat ³² 1948	A 28 year old patient died in the 3rd month of gestation after a 4 day fever. Culture of the blood

TABLE 5—*Continued*

	urine, stool and cervix were positive for <i>E. coli</i> . She died 33 days later. Fetal stem culture from the pericardial fluid and lungs were positive for <i>Pseudomonas</i> and <i>E. coli</i> .
Hill 1949	A 28 year old primigravida was infected in the 10th month of pregnancy because of preeclamptic toxemia. She was delivered of a stillborn female and a male who died 24 hours. <i>Pseudomonas</i> was cultured from the patient's blood serum and cervix and he died after 4 months illness with <i>Pseudomonas</i> septicemia.
Vincent and Cannon 1952	A 29 year old primigravida had diarrhea for 1 month prior to abortion at 5 months gestation. She died in the 33rd hospital day having had ethereal mummification of her body. <i>Leishmania</i> was cultured from the placenta, amniotic fluid, kidney, lungs, and spleen. The infant appeared normal but died 2 hours after birth with intensely congested liver and spleen. <i>Pseudomonas</i> was recovered from the infant's liver, spleen, bone marrow and meconium.
Hoffman 1951	A male twin infant was dematierythemic and cyanotic and died 4 days after birth. <i>Leishmania</i> was cultured from the pleural cavity. The infant also had meningitis and myocarditis. The mother was well.
Korte 1959	The mother had nephritis after the 6th month of pregnancy. A full-term male infant died on the 4th day with dyspnea, cyanosis and skin macule. <i>Leishmania</i> was cultured from the infant's middle ear, liver, spleen, kidney and pleura.
Stoohs and Schenck 1956	2 cases. A 38 year old multipara had chills and fever for 2 days and aborted a 3 1/2 month fetus. Her blood culture was positive for <i>Leishmania</i> but the fetus was improved and excreted. The fetus was infected.
	A 22 year old multipara was delivered of a stillborn male at 36 weeks gestation. She had chills, nausea, vomiting, high fever, pleural effusion and sputum were positive for <i>Pseudomonas</i> which was also grown from the placenta and pleura of the infant.

TABLE 5—Continued

Walthard ²⁵⁵ 1904	A 35 year old multipara with chill and fever 3 days postpartum <i>Pseudomonas</i> was cultured from the lochia along with other organisms. The patient recovered.
Rolly ²⁶³ 1906	Following a septic and incomplete abortion <i>Pseudomonas</i> was cultured from the patient's blood and spinal fluid. She died on the 11th day. <i>Pseudomonas</i> was cultured from the heart valve and most of the body organs.
Delmotte ⁹ 1910	An 18 year old primipara was febrile 2 days after spontaneous delivery. <i>Pseudomonas</i> was cultured from the lochia but blood cultures were negative. The patient recovered.
Noifer 1928	A 34 year old multipara with pain, fever and chill following incomplete septic abortion was induced and the product of a 2 month gestation recovered. <i>Pseudomonas</i> was cultured from the blood and placenta. She recovered.
Gaucheraud and Figeaud ³ 1928	The mother had septic endometritis at delivery but recovered in 10 days. 4 days after delivery the infant developed meningitis and hydrocephalus. <i>Pseudomonas</i> was cultured from the ventricular aspirate and the infant died on the 37th day (? contaminated spinal tap).
Allin ⁴ 1941	A 27 year old patient had fever, vomiting and diarrhea during delivery of a premature infant (34 week). <i>Pseudomonas</i> was cultured from the mother's stool. She recovered and was discharged after a 1 month illness. On the 5th day the infant developed red macular areas over the body and died with <i>Pseudomonas</i> meningitis.
Krau and Hunter 1941	The patient had enteritis the day before and chill during delivery. Stools were positive for <i>Pseudomonas</i> . The infant died 20 hours later with cyanosis, dyspnea, leukocytosis and a macular rash. Culture of the infant's blood, pleural exudate and brain exudate were positive for <i>Pseudomonas</i> .
Keefer and Hewitt ²⁶⁶ 1946	No clinical details. The patient died.
Solbi and Mizrat ²⁶⁷ 1948	A 28 year old patient aborted in the 3rd month of gestation after a 2 day fever. Cultures of the blood

TABLE 6—4 Clinical Lists of Reported Cases of *Proteus* Infection / the *Proteus* Infection

Author	Age and Sex	Lesion	Treatment	Result	Remarks
Pawel 1889	4y 3mo				<i>Proteus</i> isolated from tularemia
Schramm 1895	3y 3mo	Acute purulent arthritis left elbow and distal rib			<i>Proteus</i> isolated from a pure patellar arthritis in a culture
Perkin 1901	3y 3mo	Acute purulent arthritis left elbow and distal rib	Resection of rib and distal age	Died	No autopsy or histological
Wassermann 1901		Arthritis knee	Amputation		
Witt 1908	OP	Knee joint and bone	Amputation	Recovered	Operation of infection unknown from knee joint
Groves 1909	3y 3mo	Secondary hip infection (after TBC) arthritis thumb	Autoclave and cure	Rapid recovery	Only the hip was cultured <i>Proteus</i> isolated
Pellet 1924	8mo	Shoulder joint	Aspiration and cure	Rapid recovery	<i>Proteus</i> isolated from joint aspirate
Miles 1930	10F	Right hip	Aspiration and cure	No change in 6 weeks	<i>Proteus</i> isolated from hip

TABLE 5—Continued

Kohn ⁴ 1957	A 42 year old gravida V aborted 3 weeks after an upper respiratory infection. The placenta was yellow and necrotic. The 7 month fetus had numerous liver and other organ abscesses culturing <i>Monilia</i> and <i>Pseudomonas</i> . The fetal blood was positive for <i>Pseudomonas</i> . There was acute phlebitis of the portal veins and adrenal hemorrhage. The mother recovered.
Pennisi et al. ^{10a} 1958	A 27 year old para 11 gravida 11 aborted a macerated infant about ten weeks before term following a traumatic douche. The vaginal discharge was greenish yellow and foul smelling. Blood cultures following antibiotic treatment were negative but <i>Pseudomonas</i> was grown from the patient's urine, lochia and from the fetal lung tissue. The mother recovered.
Meyer ^{2,8} 1960	A 25 year old female was hospitalized for elective cesarian section 1 week prior to term. She was catheterized and sectioned under spinal anesthesia giving birth to a viable male infant. Several days later she became febrile, toxic, hypotensive, went into pulmonary edema and died with ventricular fibrillation. Antemortem cultures of blood and urine were positive for <i>Pseudomonas</i> . Autopsy showed unilateral renal papillary necrosis with suppurative pyelonephritis and obstructing calculus in the left ureter.

The portal of entry in many cases has been the birth canal. Several of the lack complete documentation. However, it is apparent that systemic infection with *Ps. aeruginosa* constitutes a serious threat to the pregnant woman and her fetus.

OSTEOMYELITIS AND ARTHRITIS

Reports of arthritis and osteomyelitis due to *Ps. aeruginosa* are uncommon. Involvement of bones and joints in most cases can be attributed to hematogenous dissemination. Stanley^{40a} in 1947 collected 10 cases from the literature. Additional reported cases are summarized with the previously reported cases in TABLE 6. Not in

TABLE 6—*Continued*

<i>Author</i>	<i>Age and Sex</i>	<i>Lesion</i>	<i>Tissue</i>	<i>Recovery</i>	<i>Remarks</i>
Herrill and Nelson 1945		Osteomyelitis	Streptococcus	Failure	No infection
Kurz 1947		Osteomyelitis			Following surgical operation on iliac crest
Flacey et al. 1947		Sequestra from osteomyelitis of femur	Atypical	Recovered	53 air-borne battle casualties with 63 lacerated wounds—mainly pen fractures of tibia—Pseudomonas found in 18 specimens (2 in pure culture)
Rehmann et al. 1949	7M	Osteomyelitis of humerus	Streptococcus	Recovered	Organism encapsulated
Cornale and Wagman 1950	58M	Pyoarthritis of knee	Streptococcus locally, and partially	Recovered	Followed abscess—infected with leukocytes grown from knee
Glanz et al. 1950	3 mo M	Arthritis of hip and left femur	Local injection of streptomycin	Recovered	Metastatic purulent arthritis followed by battle wound on extremity in pure culture from joint aspiration
Friedenberg 1950	64M	Osteomyelitis of left thumb and arthritis of left hand	Metastatic from infected focus	Recovered	Osteomyelitis followed by osteomyelitis after surgical treatment—Urine and blood, pyogenic culture

TABLE 6—(continued)

Author	Age and Sex	Lesion	Treatment	Result	Remarks
Thompson 1938	31 M	Right ankle joint and tibia	Incision and drainage	Rapid recovery	Burn of extremity followed by ulceration abscesses Pseudomonas in joint pus
	15 mo later	Right ankle	Incision and drainage auto venous vaccine	Healed in 2 weeks	
Kuon and 1938	15 M	Osteomyelitis tibia D9 10 11	No data	No data	Daily catheterization for tracture followed by pyelonephritis and abscesses—Pseudomonas in abscess and in urine
Bormis 1939		Acute osteomyelitis of sternal manubrium	Sequester removed (Pseudomonas grown)	Rapid recovery	From septic spread of furuncle on right arm—not cultured
Wheeler 1940	56 M	Osteomyelitis tibia (D7 8) ? abscess medullary tumor	Sulfa	Slow recovery	Had bacteremia after cystoscopy for renal lithiasis. Urine and blood positive for Pseudomonas
Fletcher 1942	7 M	Chronic arthritis	Oral vaccine	No relapse for 3 years	Had a transient final Pseudomonas but no evidence of suppurative arthritis
Burdick 1945	60 M	Abscess tibia	Radical excision	Recovered	Pseudomonas bacteremia after urinary catheterization—Lesion appeared after upper abdominal surgery

TABLE 6—Continued

Author	Age and Sex	Lesion	Treatment	Result	Remarks
Apley 1954	9 mo M	Osteomyelitis of tibia			
Leigh et al. 1955	63M	Osteomyelitis of spine L1, 2, D7, 8	Antibiotics	Resolved slowly	Following operation for renal calculus—Pseudomonas pirated from bone lesion
Henson and Cooley 1956	50M	T11, 12 and L1, 2 and adjacent vertebrae	Immobilization with cast Corticosteroids and x-ray	Solid bone fusion in 6 months	Cystic degeneration for ureterolithiasis 7 months previously. Pus from L grew Pseudomonas
Watkins 1957	2 wk F	Osteomyelitis right humerus	Sterilization oxytetracycline gammaglobulin		Exchange transfusion for erythroblastosis fetal 2 weeks later osteomyelitis developed

TABLE 6—Continued

Author	Age and Sex	Lesion	Treatment	Result	Remarks
Coleman and Lowry ¹⁷ 1941	Immature infant	Purulent knee	Streptomycin	Recovered	Source unidentified (Pseudomonas isolated)
Walker ¹⁸ 1942	7 mo M	Osteomyelitis, tibia; lateral	Polymyxin B in incision drainage curettage	Recovered	Followed marrow infiltration (Pseudomonas isolated)
Jawetz ⁴ 1942	2½	Purulent arthritis	Polymyxin B locally	Recovered	No details
		Osteomyelitis, roof of left orbit	Polymyxin B intrathecal	Recovered	Had abscess in meninges secondary to skull fracture and burr hole
Yarrow ¹⁹ 1942		No details			
Kreitner ²⁰ 1949	53M	Osteomyelitis, sacrum	Blood transfusion and antibiotics	Recovered	Had operation for cancer of rectum—developed abscess in sacral wound cavity
Manoukian ²⁴ 1953	60M	Osteomyelitis, tibia with sequestrum	Polymyxin B local and intramuscular incision and drainage	Recovered	Occurred 1 month after surgical procedure to treat myeloma (Pseudomonas isolated)

TABLE 6—*Continued*

<i>Author</i>	<i>Age and Sex</i>	<i>Lesion</i>	<i>Treatment</i>	<i>Result</i>	<i>Remarks</i>
Krepler ¹ 1954	910 M	Osteomyelitis of pne			
Leigh et al. ¹ 1955	63M	Osteomyelitis of spine L1-2 D7-8	Antibiotic	Recovered slowly	Following operation for renal calculus—1 pseudomonas aspirated from bone lesion
Henon and Coentry ¹ 1956	50M	T11-12 and L1 and adjacent vertebrae	Immobility with cast Cervical thoracic and x-ray	Sold slowly fusion in 6 months	Cystic copy for ureterolithiasis 7 months previously Pus from L grew Pseudomonas
Wahren ¹ 1957	2 wk F	Osteomyelitis right humerus	Streptomycin oxytetracycline gamma globulin		Exchange transfusion for erythro- blastosis fetalis 2 weeks later osteomyelitis developed Recovered



FIG. 16—*Ps. aeruginosa* arthritis. A aspiration from the swollen left knee was productive of a thin non-anomalous pus from which *Ps. aeruginosa* was obtained several times on culture.

cluded in the listed cases are suppurative processes in the region of the mastoid often associated with otitis media due to *Ps. aeruginosa*. Occasional cases¹¹⁷ are not tabulated because of insufficient data. Pseudomonas infections of bones and joints are frequently preceded by urinary infections.

Lame¹¹⁸⁻¹²⁰ who considers osteitis pubis to be an osteomyelitis has postulated a series of lesions involving bones and joint which may result from dissemination of infections of the urinary tract. This sequence involves consecutively osteitis pubis, purulent infection of the hip joint and vertebral osteomyelitis. He found in the literature three patients reported to have osteitis pubis who subsequently developed arthritis of one or both hips.¹²¹⁻¹²³ Only one of the lesions was cultured and *Ps. aeruginosa* was recovered both from the hip and from the urine. All 3 cases and a fourth presented by the author occurred following prostatectomy.



Fig. 17—An X-ray film of the distal femur of the patient illustrated in Fig. 16. Large osteolytic defects involving the epiphysis and cortex are apparent.

Listed in TABLE 6 are several reported cases of spinal and pelvic osteomyelitis due to *Ps. aeruginosa* which followed operative procedures on the urinary tract. Since it is usual for roentgenographic demonstration of such lesions to lag weeks or months behind symptomatic onset, specific identification of the causal agent in many cases depends on aspiration smear and culture of the osseous lesion itself.



18

FIG. 18.—*Pseudomonas* colonies, synovial surface, right hip, causing acute arthritis. Hematoxylin-eosin ($\times 380$).

It has been pointed out by Leigh et al.⁶⁹ that in such cases the entire spinal column should be examined for multiple lesions.

We have followed the clinical courses of 3 patients with infections of joints due to *Ps. aeruginosa*. One of them, a 5-year-old male with acute lymphocytic leukemia, insidiously developed a painful, swollen left knee with associated high fever (see FIGURE 16). The initial aspirated material contained many polymorphonuclear cells but was sterile. All subsequent aspirations were positive for *Ps. aeruginosa*. No osteomyelitis could be demonstrated. The situation

suggested bacterial contamination at the time of the initial procedure. However, a large osteolytic defect in the adjacent distal femur with epiphyseal involvement and cortical destruction which originally was considered to be an atypical leukemic lesion proved on biopsy and culture to be osteomyelitis due to *Ps aeruginosa* (see FIGURE 17). Attempts at conservative therapy including local irrigation with polymyxin B together with systemic antibacterial therapy were unsuccessful. Subsequent incision and drainage of the knee joint with curetting of the osteolytic lesion and immobilization of the joint resulted in negative cultures and a slow but definite clinical improvement.

FIGURE 18 illustrates colonies of *Ps aeruginosa* on the synovium of the right hip joint of a patient with chronic leukemia who had acute septic arthritis with pseudomonas septicemia.

EYE

Since 1885 when infection of the eye due to *Ps aeruginosa* was first reported in the form of dacryocystitis, destructive lesions in various forms caused by this organism have been described. Spencer's article on *Ps aeruginosa* infections of the eye includes an extensive list of references on this topic.⁴⁰ The most common form of eye infection is corneal ulcer which may spread with alarming rapidity to become panophthalmitis. The first recognized case was reported by Sattler³¹⁹ in 1891. A typical history is that of minor abrasion or foreign body followed in one to three days by the appearance and rapid growth of a white ulcer with a characteristic area of necrosis and a semitransparent center. The bacteria migrate rapidly from the corneal tissue into lymph spaces.⁴¹ The organisms multiply rapidly at the point of entry, extend into the normal cornea and cause widespread destruction as they form endotoxins and exotoxins.⁴²

⁴³ Such infections are notoriously resistant to therapy and are recognized to be among the most serious corneal lesions.⁴³⁻⁴⁶ Prior to the advent of sulfonamides loss of vision with or without enucleation was the common result. Infection may also take the form of conjunctivitis,¹⁰¹ necrosis of the eyelids,¹⁴⁴⁻¹⁴⁷ dacryocystitis,⁴¹⁰ punctate

keratitis meibomitis and endophthalmitis. Contaminated medicinal solutions have been implicated in some cases.¹³⁷⁻¹⁴⁰

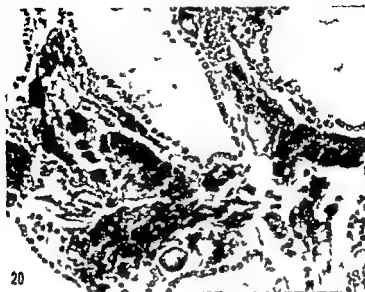
Fisher and Allen¹³⁴ have recently investigated the role of protease in ocular damage due to *Ps. aeruginosa*. They have noted a correlation between the proteolytic capacity of the strain and the degree of corneal ulceration. Severe corneal damage was produced in animals utilizing a cell free preparation containing a protease or possibly more specifically a collagenase. Further immunologic studies by these authors^{134b} suggested to them that antibodies may be produced against these enzymes with interesting therapeutic implications.

EAR

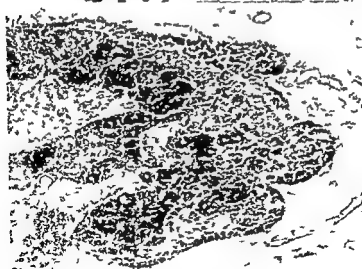
Prior to 1940 the principal organisms cultured from otitis externa lesions were fungi of one type or another. Since then it has been shown that gram negative bacteria, specifically *Ps. aeruginosa*



FIG 19—Otitis media due to *Ps. aeruginosa*



20



21

FIG. 20—(a) c) Int r t t a l l u l r n a o l o m t h y o t g l a n d H m t x y l o
($\times 210$)

FIG. 21—(b l o w) l e l m l y n g l a d n t t h e n t y h n e s m ($\times 75$)

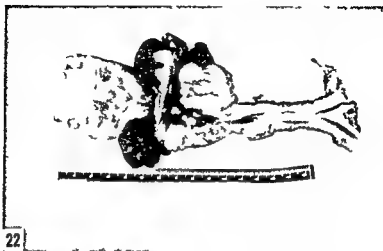


FIG 22—(above) Necrotic hemorrhagic tonsil due to *Pseudomonas aeruginosa*

FIG 23—(below) Focal necrosis due to *Pseudomonas aeruginosa* cultured from the tonsil (hematoxylin-eosin, $\times 12$)

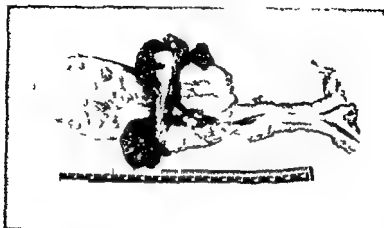
are frequently present. Persistent infection may develop particularly in moist tropical climate.^{111 112 113 114 115} Complications such as abscess of the brain³⁷³ meningitis and thrombophlebitis of the lateral sinus occasionally occur and several cases have been associated with meningitis either by direct extension or by way of the blood stream.^{7 100 144 147 11 7 48 33}

One of our patients developed otitis media due to *Ps. aeruginosa*. The histologic picture may be seen in FIGURE 19. It is not known whether this was a primary or secondary infection for the patient died with disseminated lesions.

MISCELLANEOUS INFECTIONS

Some of the more frequent and more prominent sites of infection due to *Ps. aeruginosa* have been discussed in detail. However many other regions of the body may be involved. Some of these include Ischiorectal abscesses^{100 119 144 147 41 3} abscesses of the liver^{1 11 447} subhepatic³³ and subphrenic abscesses³ abscesses of the thyroid gland⁴⁵⁷ gastrointestinal ulcerations⁴ abscess of the brain^{7 340 373} gallbladder⁶ cholangitis³⁸ pelvic abscess³³ epiphagitis¹⁵ abscess of the parotid gland⁶³ dental caries⁹ pericarditis¹ peritonitis^{69 10 1 33 0 64 6 213} multiple metastatic abscesses³⁶ arteriovenous fistula⁸⁷ and pulmonary arteritis¹⁷³.

Additional infections in our own series either primary or secondary are illustrated by photographed microscopic sections of the thyroid gland (FIGURE 20) lymph node (FIGURE 21) and tonsil (FIGURES 22 and 23) on the preceding two pages.



22



23

FIG 22—(above) Necrosis in, hemorrhagic tonsillitis due to *Ps. aeruginosa*

FIG 23—(below) Tonsil cross section due to *Pseudomonas aeruginosa* (faucial tonsil)
Hematoxylin-eosin ($\times 17$)

of references dealing with data on toxicity resistance antibiotic synergism and in vitro testing is available in Jawetz monograph¹

SYSTEMIC INFECTION

Bacteremia or endocarditis due to *Ps aeruginosa* should be treated immediately with polymyxin B which is probably the drug of choice^{10 11 40 461} In the presence of good renal function prolonged therapy with polymyxin B in full dose is probably safe¹⁰ Recommended doses are 1.5 to 2.5 mg/kg/day in 3 or 4 equal intramuscular injections for two weeks with a daily maximum of 200 mg Polymyxin B has been given both intramuscularly and intravenously for extended periods in at least one case of endocarditis without evidence of permanent toxicity In the presence of pre existing renal disease a maximum dose of 1.0 to 1.5 mg/kg/day with careful clinical and laboratory supervision is indicated One per cent procaine solution may be added to minimize local irritative effects Oxytetracycline may act synergistically with polymyxin and probably should be administered concurrently in oral doses of 250 mg 4 times daily Sensitivity studies should be performed in all cases although this should not delay the institution of appropriate treatment Neomycin may prove valuable in some cases Polymyxin has been given intravenously (200 mg in 2000 ml of fluid) but this route of administration needs further evaluation

URINARY INFECTIONS

Polymyxin is probably the drug of choice in acute and chronic urinary tract infections due to *Ps aeruginosa*^{10 11 40 461} This should be given intramuscularly in full doses possibly in conjunction with oxytetracycline Local urethral or bladder irrigation of polymyxin solutions may be useful in some cases

INTRATHECAL ADMINISTRATION

Since polymyxin does not cross the blood brain barrier⁴¹ the route of choice for *Pseudomonas meningitis* is intrathecal Jawetz

3 Antibiotic Therapy

Several excellent sources of information about the treatment of infections due to *Ps. aeruginosa* with polymyxin B are available.⁴

⁴³⁰ ⁴⁴ ⁴⁶¹ Much of the following data can be found in a monograph by Jiwetz⁴⁵ and in an article by Waisbren.⁴³

The polymyxins originally reported in 1917^{40b} are basic polypeptides with a relatively narrow antibacterial spectrum. Their action is predominantly against gram-negative organisms and is bactericidal. Most strains of *Pseudomonas* are inhibited in vitro by a concentration of polymyxin B of 2.0 micrograms per milliliter or less.⁴⁶ Development of resistance is uncommon in originally susceptible strains. Cross-resistance with other antibiotics has not been encountered. Detailed studies on the action of polymyxin against *Ps. aeruginosa* are available.^{3, 40, 41}

Absorption by the oral route is insignificant, but usefulness as the sole agent for preoperative sterilization of the bowel is limited by its narrow spectrum of activity. No significant blood or urine levels are obtained after topical application.⁴ By the intramuscular route the drug is well absorbed and distributed, reaching an effective level in the blood in one half hour and a peak in two hours. The optimum bactericidal effect of polymyxin B is obtained when sufficient concentrations of the drug are brought into direct contact with the source of actively multiplying organisms. Since transfer of polymyxin from the bloodstream into body cavities is often impaired, it becomes essential to select the appropriate route of drug administration for maximum therapeutic effect.

Dosage and duration of treatment is also of great importance since neurotoxic and nephrotoxic effects have been reported. The effects appear to be transient within the recommended dosage schedule, but in the presence of renal disease with elevated non-protein nitrogen serum levels may accumulate, necessitating careful clinical and laboratory supervision of therapy. After parenteral administration polymyxin is largely excreted in the urine. A fairly complete list

this time.⁶ Intrapleural administration of polymyxin for the treatment of empyema may be of value with or without the use of enzymatic agents. Irrigation of infected wounds, sinuses, or joints with solutions of 1 to 10 mg polymyxin B per ml sterile saline has been of therapeutic value when combined with adequate drainage or enzymatic debridement.

THERAPY WITH COLISTIN SALTS

Recent reports in the American literature^{179-300, 384, 385} indicate that a new antibiotic colistin produced by *Aerobacillus colistinus* may prove useful in the treatment of pseudomonas infections. Colistin was first reported in 1950 by Koyama and his associates.⁴⁸ The two commercially available forms⁸ are colistin sulfate (Coly Mycin S) the oral form and sodium colistin methanesulfonate (Coly Mycin M) an intramuscular preparation. Much of the investigation to date has been carried out in Japan and Italy. A good bibliography is listed by Schwartz et al.³⁹¹ The cyclic polypeptide compounds appear to have a similar spectrum and activity to that of polymyxin B, however, probably without serious nephrotoxic features. Preliminary studies indicate that for *Ps. aeruginosa* these new drugs are rapidly bactericidal; sensitive strains do not readily develop resistance, and there is no cross resistance with the broad spectrum antibiotics.

Graber et al.¹⁷⁹ found *Ps. aeruginosa* to be highly sensitive to colistin sulfate; only 5 of 18 strains requiring a plasma level as much as 3.12 µg/ml for bactericidal activity. They recommend its use in pseudomonas septicemia complicating severe burns. McCabe et al.³⁰⁰ found colistin valuable in the treatment of wound infections due to *Ps. aeruginosa*. Lack of nephrotoxicity was confirmed, but the effect against pseudomonas was less uniform than that of polymyxin B.

Gastrointestinal absorption of colistin is negligible except possibly in small infants. Ross et al.³⁸⁴ suggest that for the pediatric age

The trade names in parentheses are the property of Warner Chilcott Laboratories.

recommends the use of 5 mg of the sterile powder dissolved in 10 ml of saline to give a final concentration of 0.5 mg per ml. This is injected daily for 3 days then every other day for a total of 10 to 15 injections.⁴³⁰ Procaine must not be added. The total daily dosage must not exceed 5 to 10 mg for adults or 2 mg for small children. Treatment should continue for at least two or three weeks after obtaining negative spinal fluid culture. The additional use of intramuscular polymyxin 50 mg 4 times daily has been suggested by some authorities.⁴³⁰ Neomycin and Streptokinase Streptodornase has been used successfully in some cases.^{101, 4} Experimental reports of the effects of intracisternal injection of polymyxin are available.^{40, 4b}

ORAL ADMINISTRATION

Tablets containing 50 mg of polymyxin B are available for oral administration. The daily adult dosage is 400 to 600 mg in divided doses.⁴ For small children 15 to 20 mg/kg/day for 10 days is suggested for the treatment of diarrhea caused by *Ps. aeruginosa*. Descriptions of clinical cases are available.^{310, 370, 433, 44} A suggested dose for the treatment of carriers has been 0.5 gm four times daily.^{431a}

TOPICAL ADMINISTRATION

Polymyxin has found wide use in the treatment of burns infected ulcers and large wounds.^{1, 46, 43f} A concentration of 0.5 to 1.0 mg per ml either alone or with neomycin or bacitracin has been useful in preventing secondary infections. No significant blood or urine levels are obtained after topical application to large burns.⁴ Similar concentrations have been used with success for the topical treatment of otitis externa due to *Ps. aeruginosa*.³⁹⁶ Polymyxin is urgently indicated for the treatment of corneal ulcer. 20 to 25 mg/day subconjunctivally has been recommended.^{210, 383, 317, 361, 419}

MISCELLANEOUS INFECTIONS

Treatment of infections of the respiratory tract with aerosol has been reported⁴⁶ but cannot receive unqualified recommendation at

4 Pathology

The characteristic pathologic lesion of *Ps. aeruginosa* infection is a diffuse acute vasculitis in which the wall of small arteries and veins are extensively invaded by pseudomonas organisms (FIGURES 2-3). This process is associated with extravascular hemorrhage and intravascular thrombosis. There is bland hemorrhagic necrosis of the surrounding tissue. Such lesions were extensively described by Fraenkel^{11, 12} and subsequent reports have served to elaborate and confirm his observation.¹³ Arteries supplied by these infected vessels become necrotic and typically assume the appearance of hemorrhagic gangrenous ulcer. The close relationship of bacteria to blood vessels apparently favors dissemination of infection. Secondary lesions are usually hemorrhagic and necrotic and are almost always non-suppurative.

The pathologic lesions of pseudomonas may be found at any or all of the various portals of entry of infectious agents into the body. They include the mouth, pharynx, middle ears, larynx, lungs, esophagus, stomach, intestines, genitourinary tract, and skin. In some cases the organism may be introduced into the spinal canal by needle or into the bladder by catheter or into the central nervous system by penetrating injury. Cellulitis in our own experience has followed the aspiration by needle of bone marrow at the iliac crest.

In 22 subjects autopsied at the Clinical Center during the period of 1954 to 1957 histopathologic lesions of *Ps. aeruginosa* were found with the following frequency: skin and subcutaneous tissues 10, lungs 9, oral mucous membranes and intestine 5 each, kidney, esophagus and myocardium 3 each, spleen, liver, pancreas, thyroid gland and paranasal sinuses 2 each, and pericardium, hip joint, pleura, middle ear and conjunctiva single instances. By contrast the distribution of post mortem cultures in the same subjects was: heart blood 13 (2 other patients had sterile cultures and 7 were not cultured), lung 1, spinal fluid 5, subcutaneous tissue and pericard

group an oral dose of 15 mg /Kg daily in an eight hour dosage schedule would be ample. Guarardo¹⁴⁴ has reported powerful activity of colistin against gram negative bacteria in the intestinal flora. He found that infantile diarrhea responded well. This has also been the experience of others.¹⁴⁵

Clearly these compounds show promise in the treatment of infections caused by *Ps. aeruginosa* and deserve further evaluation.

At this time it is difficult to assess in any specific way what the anticipated results of a given therapeutic regimen should be. Large series of patients treated comparably are not available for analysis in most types of infection due to *Ps. aeruginosa*. However it does seem clear that systemic or meningeal infection is always serious and carries a poor prognosis particularly in the absence of adequate natural body defense mechanisms. Local infections on the other hand frequently respond favorably when recognized early and treated appropriately.

4 Pathology

The characteristic pathologic lesion of *Ps aeruginosa* infection is a diffuse acute vasculitis in which the wall of small arteries and veins are extensively invaded by pseudomonas organisms (FIGURES 2-3). This process is associated with extracellular hemorrhage and intravascular thrombosis. There is blind hemorrhagic necrosis of the surrounding tissue. Such lesions were extensively described by Fraenkel^{144, 145} and subsequent reports have served to elaborate and confirm his observations.¹⁴ Arteries supplied by these infected vessels become necrotic and typically assume the appearance of hemorrhagic gangrenous ulcers. The close relationship of bacteria to blood vessels apparently favors dissemination of infection. Secondary lesions are usually hemorrhagic and necrotic and are almost always non-suppurative.

The pathologic lesions of pseudomonas may be found at any or all of the various portals of entry of infectious agents into the body. They include the mouth, pharynx, middle ear, larynx, lungs, esophagus, stomach, intestines, genitourinary tract, and skin. In some cases the organism may be introduced into the spinal canal by needle or into the bladder by catheter or into the central nervous system by penetrating injury. Cellulitis in our own experience has followed the aspiration by needle of bone marrow at the iliac crest.

In 22 subjects autopsied at the Clinical Center during the period of 1954 to 1957 histopathologic lesions of *Ps aeruginosa* were found with the following frequency: skin and subcutaneous tissues 10, lung 9, oral mucous membranes and intestine 5, each kidney, esophagus and myocardium 3, each spleen, liver, pancreas, thyroid gland and paranasal sinuses 2, each and pericardium, hip joint, pleura, middle ear and conjunctiva single instances. By contrast the distribution of post mortem cultures in the same subjects was: heart blood 13 (2 other patients had sterile cultures and 7 were not cultured), lung 8, spinal fluid 5, subcutaneous tissue and pericard

group on oral dose of 15 mg/kg daily in an eight hour dosage schedule would be ample. Cur sardo¹⁴ has reported powerful activity of colistin against gram negative bacteria in the intestinal flora. He found that infantile diarrheas responded well. This has also been the experience of others.¹⁵

Clearly the new compound is how promising in the treatment of infections caused by *Ps. aeruginosa* and deserve further evaluation.

At this time it is difficult to assess in any specific way what the anticipated results of a given therapeutic regimen should be. Large series of patients treated comparably are not available for analysis in most types of infection due to *Ps. aeruginosa*. However it does seem clear that systemic or meningeal infection is always serious and carries a poor prognosis, particularly in the absence of adequate natural body defense mechanisms. Local infection on the other hand frequently respond favorably when recognized early and treated appropriately.

5 Summary

A review of infections caused by *Ps. aeruginosa* has been presented. What general principles can be derived from this collected information and how can they be specifically applied? Which areas of investigation will be most rewarding in terms of increased knowledge of the organism and better clinical management of the patient?

First of all there must be general recognition that *Ps. aeruginosa* is potentially pathogenic for man. Infection is most likely to occur in a setting where body defense mechanisms are immature as in infants or overtaxed as in patient already debilitated from some other cause. Therapeutic measures designed to combat one condition may provide an environment favorable for the establishment of resistant pseudomonas infections. Examples of this are numerous and include prolonged administration of antibiotics, the use of ionizing radiation and chemotherapeutic agents in neoplastic disease and in kidney transplantation the employment of venous and urinary catheters, the use of pump oxygenators for extracorporeal circulation in cardiac surgery and the use of lumbar puncture for diagnostic or therapeutic reasons. These procedures are often useful and necessary but have introduced problems which must be anticipated, recognized and treated effectively.

Ps. aeruginosa is ubiquitous and may thrive in the usual antiseptic solutions used for preparing skin, storing catheters and other surgical instruments.^{10, 11, 12, 13, 14, 15} The antibacterial activity of such solutions may diminish over a period of time to encourage this growth.^{16, 17} Bed pans and urine bottles are the most likely sources for contamination of the hands of ward personnel.¹⁸ In this regard carbolic acid as a 2 per cent solution has been reported to be an effective antiseptic.

With the possible exception of direct introduction of organisms into the blood or spinal fluid, serious infection with pseudomonas would appear to be uncommon in non debilitated adult. It is the susceptible patient for whom strict precautionary measures must be

ial fluid 3 each ascitic fluid synovial fluid and intestine 2 each and oral mucous membrane pleural fluid kidney spleen liver middle ear paranasal sinuses eye nose and lip single instance. The considerable differences between the histopathologic and bacteriologic distribution are attributable to differences in sampling.

The significance of a post mortem culture of pseudomonas is much greater than is the significance of bacterial contaminant such as *E. coli*. Fraenkel found only 75 instances of positive pseudomonas cultures among 6646 positive blood cultures in 11286 autopsies. Since pseudomonas usually outgrows other bacteria in contaminated material and is so infrequently present in post mortem culture positive autopsy cultures of this organism are highly significant and should serve to alert the pathologist to search the tissues carefully for evidence of invasion. In 1922¹⁴⁷ Fraenkel remarked that scarcely an organ in the body had not been at one time or another described as the site of pseudomonas infection.

5 Summary

A review of infections caused by *Ps aeruginosa* has been presented. What general principles can be derived from this collected information and how can they be specifically applied? Which areas of investigation will be most rewarding in terms of increased knowledge of the organism and better clinical management of the patient?

First of all there must be general recognition that *Ps aeruginosa* is potentially pathogenic for man. Infection is most likely to occur in a setting where body defense mechanisms are immature as in infants or overtaxed as in patients already debilitated from some other cause. Therapeutic measures designed to combat one condition may provide an environment favorable for the establishment of resistant pseudomonas infections. Examples of this are numerous and include prolonged administration of antibiotics, the use of ionizing radiation and chemotherapeutic agents in neoplastic disease and in kidney transplantation, the employment of venous and urinary catheters, the use of pump oxygenators for extracorporeal circulation in cardiac surgery, and the use of lumbar puncture for diagnostic or therapeutic reason. These procedures are often useful and necessary but have introduced problems which must be anticipated, recognized, and treated effectively.

Ps aeruginosa is ubiquitous and may thrive in the usual antiseptic solutions used for preparing skin, storing catheters and other surgical instruments.^{30a, 31, 32, 33, 42} The antibacterial activity of such solutions may diminish over a period of time to encourage this growth.³⁴ Bed pans and urine bottles are the most likely sources for contamination of the hands of ward personnel.³⁰ In this regard carbolic acid as a 2 per cent solution has been reported to be an effective antiseptic.

With the possible exception of direct introduction of organisms into the blood or spinal fluid, serious infection with pseudomonas would appear to be uncommon in non-debilitated adults. It is the susceptible patient for whom strict precautionary measures must be

taken. These should include isolation from known sources of infection and frequent changes of antiseptic solutions or other possible bacterial reservoirs. The more susceptible the patient is judged clinically, the more stringent should be the precautions. Antibiotics, particularly broad spectrum drugs, should be withheld in the absence of specific indications. Prolonged and prophylactic treatment with antibiotic agents is to be discouraged. Strict attention to bed sores, particularly those near the urogenital area, is important since these may offer a convenient portal of entry to the bloodstream. The presence of oral moniliasis may indicate the existence of an environment favorable to pseudomonas, since the organisms frequently occur together. The appearance of characteristic cutaneous lesions or less specific signs such as fever, jaundice, unexplained neurologic symptoms or sudden shock may herald the onset of septicemia. Other clinical features of infection have been discussed. Cultures should be taken from suspicious areas and sensitivities performed.

Major problems in the management of pseudomonas infection have been (1) the apparent inability of the host to summon adequate natural body defenses and (2) the resistance of the organisms to available therapeutic agents. Polymyxin B and neomycin or possibly colistin appear to be drugs of choice in most cases. The early institution of appropriate therapy for a sufficient period of time is vital since pseudomonas infections tend to assume a chronic and relapsing course.

Several areas require further investigation. Rapid, simple methods of bacteriologic identification are needed. Studies on modes of transmission are suggestive but not conclusive. The relation of cutaneous lesions to the Schwartzman phenomenon is of interest and not well understood.⁴³ The mechanism of leukopenia and of shock has been studied but needs further clarification, particularly with reference to the role of circulating endotoxin. The role of adrenal cortical steroids as a possible predisposing factor is of interest and difficult to evaluate. The use of these compounds in the treatment of bacteremic shock due to *Ps. aeruginosa* has not been successful in our hands.¹⁴⁰ The status of gamma globulin needs

investigation. In our own experience in patients with leukemia, serum levels of gamma globulin did not change significantly with the onset of pseudomonas infection. Rothenthal et al.³⁶³ rendered mice susceptible to pseudomonas infections by pretreatment with cortisone and were able to protect the animals by administration of human gamma globulin. A synergistic effect was obtained by the combination of oxytetracycline with gamma globulin or plasma.³⁶⁴ Other studies on the potentiating effects of gamma globulin are available.^{134, 173, 44} The role of phagocytic action on pseudomonas infection in mice is being studied.³⁶⁵ Investigations of the properdin system may be useful in our understanding of natural body defenses.³⁴³ Possibly the best attack would be the most direct, namely the discovery of an antibiotic agent specific in its action against these organisms and without deleterious side effects. The colistin salts or related compounds may provide this need. Meanwhile the intelligent application of already established principles should prevent or abort many of the resistant infections due to *Ps. aeruginosa*.

References

- 1 ABADIE J AND LAROCHE G Un cas de meningite pyocyanique traitée et guérie par l'auto-éra-thérapie intrarachidienne Bull Acad nat med 80 15 1918
- 2 AGULNIK M Primäre eitrige Pyocyaneus Meningitis bei einem jungen Kinde Ann paediat 167 38 1946
- 3 ALKILWICZ J MAJEWSKI C AND JANIAKOWA E O działaniu antybiotycznym pałeczki ropy błękitnej na grzyby charakteryzowane (Antibiotic action of Pseudomonas aeruginosa on pathogenic fungi) Przeł dermat Warsz 4 13 1954
- 4 ALLIN A E Meningitis of the newborn due to Pseudomonas aeruginosa Canad MAJ 44 288 1941
- 5 ALPERT D R Intraocular injection of penicillin in a case of ring abscess of the cornea Am J Ophth 28 64 1945
- 5a ANDERSON K Pseudomonas pyocyanea disseminated from an air cooling apparatus MJ Australia 1 529 1959
- 6 ANDRE A DECORTIS CONSTANT M AND DOLHA H A propos des infections par bacille pyocyanique Rev med Liege 7 111 1952
- 6a ANNOTATIONS Failure of detergent to disinfect Lancet 2 306 1958
- 6b — Bacteria in antiseptic solution Brit MJ 2 436 1958
- 7 APPELBAUM E AND LEFF W A Occurrence of superinfections during antibiotic treatment JAMA 138 119 1948
- 8 — NELSON J AND ALBIN M H The treatment of pneumococcal meningitis with penicillin Am J Med Sc 218 260 1949
- 9 ARKOVY J Experimentelle Untersuchungen über Gangrän an der Zohnpulpas und Wundgangrän Zentralbl Bakt 23 917 962 1898
- 9a ASAY L D AND KOCH R Pseudomonas infections in infants and children N Eng J M 262 1062 1960
- 10 ASHBY W M ELBRIDGE W W AND FREEMAN W Chronic pyocyaneus infection - gastrointestinal localization with fatal outcome JAMA 88 1304 1927
- 11 ASHESOVA J Le bacteriophage du bacille pyocyanique et les taches urinaires Compt rend Soc de biol 95 1029 1926
- 12 ASKEY J M Bacillus pyocyaneus septicaemia (Report of a case with unusual blood findings) California & West Med 32 352 1930
- 13 BABES AND CORNILL Le bacteries ed 3 Paris Felix Alcan 1890 p 48f
- 14 BACINSKY A Zur Bacillus pyocyaneus Infektion im kindlichen Alter Zentralbl Bakt 47 427 1908
- 15 BARKER L F The clinical symptom bacteriologic findings and postmortem appearances in cases of infection of human beings with the bacillus pyocyaneus JAMA 29 213 1894
- 16 BARRON M Meningitis in the newborn and in early infancy Am J Med Sc 156 358 1918

- 17 BARTHOLOMEW J W Fluorination of certain species of pseudomonas as seen with the electron microscope J Gen Microb 3 340 1949
- 18 BATSON O V The function of the vertebral vein and their role in the spread of metastasis Ann Surg 112 138 1940
- 19 BAUER M F AND COHEN H The role of Pseudomonas aeruginosa infection about the nail A M A Arch Dermat 75 394 1957
- 20 BALMEISTER H Z m Krankheit bilde der Pyocyneuropathie beim Erwachsenen Dtsch med Wchnchr 57 1099 1931
- 21 BEDELL H AND PARRY S S Recurrent pseudomonas meningitis following intracranial meningitis New York J Med 51 1431 1951
- 21a BENEDICT R G AND LANGLEY, A F Antibiotic activity of Bacillus polymyxa J Bact 54 24 1947
- 22 BENFAY A Ueber Pyocyane Med Klin 50 1199 1907
- 23 BENNETT I L JR AND BEESON P H Therapeutic properties and biologic effect of bacterial pyocyanine Medicine 29 365 1950
- 24 BERGER E H Primary pyocyaneumeningitis Report of a case ending in recovery Northw J Med 34 42 1938
- 25 BERKA F Pyocyaneumbeund bei Meningitis W e klin Wchnchr 16 308 1903
- 26 BERNHARDT R Lebercollepyocyanin und seine Wirkung auf das Galle 0 133 1900
- 27 BEZI S Zur pathologie des Atmungstraktes bei Pyocyaneuminfektion Dtsch path Anz 92 41 1933
- 28 BHATNAGAR S S Bacillus pyocyanus and its infection J Roy Army Med Corps 63 331 1934
- 29 BIEHL J P AND HAMBURGER M Polymyxin B therapy of meningitis following pneumococcal infection of the central nervous system AM J Med 93 367 1944
- 30 DIELICKA I On the effect of Bacillus pyocyaneus infection in infants Preliminary communication Review of the literature Observations on 2 cases Treatment of Bacillus pyocyaneus infection with methylene blue Pol k tygodnik 6 18 1951
- 31 — AND DZIENISZEWSKA L Zakazanie poliklinik w Warszawie (Pseudomonas aeruginosa infection in preterm infant) Pol k tygodnik 1413 1953
- 32 BIFULCO E Primary Bacillus pyocyaneus infection in nail with erythema New York J Med 49 1195 1949
- 33 BIGNELL J L Infection of the cornea with Bacillus pyocyaneus Brit J Ophth 35 419 1951
- 33a BISETTI A AND POCCHIO G Immediate effect of neomycin on a strain of pharyngitis caused by Pseudomonas aeruginosa resistant to polymyxin B P h hnc (suppl) 65 1451 1958
- 34 BISHOP W A JR A case of primary Bacillus pyocyaneus arthritis in an infant J Pediatr 50 216 1938
- 35 BLUM S Ein Fall von Pyocyaneumkomplikation bei Pyocyaneuminfektion—Epidemiologische Ztschrift 25 113 1899

- 36 BLUMIG I Multiple Abscessen und Granulome in den Organen eines Säuglings als Folge einer *Pyocyaneus*-Allgemeinfektion Zentralbl allg Path 97 143 1951
- 37 BONZANIGO C AND MOLO C Aeroperitonäalbehandlung einer *Pyocyaneus*-Meningitis Ann J aediat Ba el 180 268 1953
- 38 BOONE J A Meningitis due to *Pseudomonas pyocyaneus*: Case successfully treated with dihydro streptomycin and sulfa J South Carolina MA 46 247 1950
- 39 BORDEN C W AND HALL, W H Fatal transfusion reactions from massive bacterial contamination of blood New England J Med 245 760 1951
- 40 BORMIOLI M Studi su di un caso di otomielite metastatica acuta purulenta del manufatto ternale da *pyocyaneus* Ann di med nav e colon 45 339 1939
- 41 POTTERALL, E H AND MACYER H Meningitis due to *Pseudomonas pyocyaneus*—penetrating wounds of the head Lancet I 112 1945
- 42 BOLCHARD C Influence qu'exerce sur la maladie charbonneuse l'inoculation du bacille pyocyanique Compt Rend Sc 109 713 1889
- 43 BOUDIN G BARBIZET J AND GUERIN C Les meninges d'inoculation a bacilles pyocyanique Semaine hop Paris 31 26 1955
- 44 BRADDE A E WILLIAMS D SIEMIENSKI J AND MURPHY R Shock like state due to transfusion of blood contaminated with gram negative bacilli—successful treatment with antibiotics and arterenol A M A Arch Int Med 92 75 1953
- 45 BRESCHY C Über ektene Zwischenfälle bei der epiduralen Novocaininjektion Klin Wchn chr 2 571 1949
- 46 BRILL N E AND LIEBMAN E *Pyocyaneus* bacillaemia: a critical review of the recorded cases with a report of a case secondary to staphylococcaemia Am J M Sc 118 153 1899
- 47 BROWN C F G *Bacillus pyocyaneus* infection Med Clin North America 14 1213 1931
- 48 BROWN E H Therapeutic experiences with corneal ulcer due to *Bacillus pyocyaneus* A M A Arch Ophth 30 221 1943
- 49 BRADBSON D F V ENTICKNAF B AND MILSTEIN B H A case of subacute bacterial endocarditis due to *Pseudomonas pyocyaneus* complicating aulotomy for advanced mitral stenosis Guys Ho p Rep 10 303 1953
- 50 BRISQ P AND BAYCOO E A Propos de deux cas de meningite a pyocyanique Med trop 11 585 1951
- 51 BULLOCK W A System of Bacteriology London Published by his majesty stationery office 1929 vol 4 pp 326-337
- 52 — AND HUNTER W Ueber *Pyocyan lysin* eine hämolytische Substanz in Kulturen des *Bacterium pyocyaneum* Zentralbl Bakt 8 865 1900
- 53 FUNGELER W Über Endocarditis maligna durch *Bacillus pyocyaneus* Frankfurt Ztschr Path 35 428 1927
- 54 BURDICK H A case of chronic metastatic abscesses of the cartilage due to *Bacillus pyocyaneus* J M S nat Ho 17 925 1945
- 55 CADEAC Contribution a l'etude de la maladie pyocyanique Compt Rend Soc Biol 2 11 1890

- 56 CAIRNS H, DUTHIE E. S. and SMITH H. V. Intrathecal streptomycin in the guinea pig: clinical trial in tuberculous coliform and the injection. *Lancet* 2 153 1946
- 57 CALMETTE A. Étude expérimentale de la dysenterie ou enterocolite disséminée d'extrême Orient et des abcès du péricardium d'Amérique. *Arch de méd nav.*, 60 207-261 335 1893
- 58 CAMERON J. D. and EDGE, J. R. Aggranulocytosis after a blood transfusion sensitization penicillin therapy of the form *Pseudomonas pyocyanea* septemia. *Br J Med* 2 688 1945
- 58a CANABILE, L., OSBORNE, W., JOHNSTON S. and BLAY P. A pattern for the in vitro and in vivo control of *Pseudomonas aeruginosa*. *Antibiot Annual* 1954-1955 New York Medical Encyclopedia Inc 1955 pp 210-218
- 59 ČANČIK J. Bacteriology in pyocyanus culture. *Časopis*, 67 25 1923
- 60 CANELLI A. F. Contributo allo studio della infezione generale da piocianeo nell'età infantile. *Pediatrics* 21 503 1919
- 61 CARNSALE P. L. and WAISMEN R. C. Rare case of *Bacillus pyocyaneus* proarthrosis. *Ann Surg* 7 939 1900
- 62 CARROLL, G., ALLEN H. N. and DOUGLY E. R. Study of bacillary infections of the urinary tract. *JAMA* 135 683 1947
- 63 CARTER H. R. *Bacillus pyocyaneus* infection cured by vaccine. *Lancet* 1 437 1904
- 64 CAWTHORNE T. D. Contribution on the chemotherapy of meningitis secondary to infection of the cerebrospinal meninges. *Proc Roy Soc Med* 9 627 1946
- 65 CHAKRAVARTI D. N. and TYAGI N. M. Pyocyanin a stimulant that of enteric fever caused by *Pseudomonas pyocyaneus* in chicks. *Indian J Med* 36 1937
- 66 CHARRI A. La maladie *Pyocyanea*. *Paris* 1881
- 67 CHAUFFARD A. and LAROCHE G. Un cas de méningite *pyocyaneuse*. *Bull de la Soc de méd trop* 1 41 645 1911
- 68 CHIRAL, H. Zur Kenntnis der *Pyocyaneus* Infektion bei Säuglingen. *Zentralbl allg Path* 38 483 1906
- 69 CHIEN J. T. T. and WIGGINS M. L. Self-inoculation with *M. tuberculosis* and *P. aeruginosa* by a diabetic woman. *Am Rev Tuberc* 69 818 1954
- 70 CHICHER E. The unusual case of meningitis in children. *J Pediatr* 43 54 1953
- 71 CHRISTIE, R. Observation on the biochemical and serological characteristics of *Pseudomonas pyocyaneus*. *Antal and JE p Biol & MSc* 26 425 1948
- 72 CIANCHI V. Reperto batteriologico nella comunità in un caso di febbre. *Boll Societ Biol* 17 05 1941
- 73 CLARKE J. M. A case of cutaneous pyocyanemia due to the *Bacillus pyocyaneus*. *Br J Med-Chir J* 31 4 1913
- 74 CLEMENT H. and MILLARD L. L'infection à *Bacille pyocyaneus* chez l'enfant. *Pediatrics* 61 661 1953
- 75 COLEBROOK L. Study of burn and scald. *Medical Research Council* (1945) Sp. C. Rep. 5. Med. P. Coun. no 249 London H.M. Stationery Office
- 76 — DUNCAN J. M. and ROSS W. P. D. The control of infection in burns. *Lancet* 1 893 1948

- 77 COLEMAN J M AND LOWRY F C Acute purulent arthritis (Bacillus pyocyanus) in a premature infant recovery with streptomycin Pediatrics 7 317 1951
- 78 COLLIER F C AND DYER D J Acute bacterial endocarditis due to Pseudomonas aeruginosa Report of a case AMA Arch Path 51 179 1951
- 79 COLLEY T B An epidemic of infantile diarrhea apparently caused by the bacillus pyocyanus JAMA 50 607 1908
- 80 CONCOS A SPARROW H STAMRAD AND ROUSSEL, H Meningite aigue a B pyocyanique at a Micrococcus catarrhalis chez un nourrisson de 8 mois Arch franç pediat 7 733 1950
- 81 COUNCILMAN W T MALLORY J B AND WRIGHT J H Epidemic cerebrospinal meningitis AmJ MSc 115 251 1898
- 82 CRICKSHANK C N D AND LOWBURY E J L The effect of pyocyanin on human skin cells and leukocytes BritJ Exper Path 31 583 1953
- 83 CURBELO A AND MARQUEZ, V Importancia de la identificacion de las cepas cromogenicas de Pseudomonas aeruginosa Rev med cubana 60 345 1954
- 84 ——— AND ——— Los antibioticos en la infeccion piocianica Rev med cubana 349 1954
- 85 ——— AND FLORES PALMA R Estudio de un gran brote Epidemic de gastroenteritis infantil de posible origen piocianico Rev med cubana 65 793 1954
- 86 CURRENCE W W Acetic acid aerosol in treatment of purulent bronchiectasis due to Pseudomonas aeruginosa AMA AmJ Dis Child 111 637 1957
- 87 CURTIN J A PETERSDORF R G AND BENNETT I L Acquired arteriovenous fistula complicated by Pseudomonas aeruginosa endarteritis and endocarditis Bull Johns Hopkins Hosp 101 140 1957
- 88 CUTLER M AND CUTLER P Pseudomonas meningitis Am Practitioner 4 200 1953
- 89 DANZ F J AND SCHULTZ E W Gelatinous variants of Pseudomonas aeruginosa J Bact 58 367 1949
- 90 DASSE H W Angerulocytic angina JAMA 91 1718 1928
- 91 DAVIDSON I M Pseudomonas pyocyanus meningitis following spinal anaesthesia Lancet 2 653 1947
- 91a DAVIS I SELLERS W ORBACH H AND WEDDINGTON G An evaluation of several media for the early detection of Pseudomonas aeruginosa encountered in clinical practice USAF Sch Aviat Med 59 14 July 1959
- 92 DE BAKEY M E AND PULASKI E J An analysis of the experience with streptomycin in United States Army Hospitals Preliminary report Surgery 20 749 1946
- 93 DE BEKARDIVIS D Ulcera corneale con ipopione da bacillus pyocyanus osservazione clinica anatomica batteriologica e sperimentale Ann di ottal Pa 32 789 1903
- 94 DEBRE, R AND MOZZICOVACCI F Streptomycin treatment of septicemia and meningitis due to intestinal organisms in infants Brit MJ 2 451 1949
- 95 ——— AND CAMIS M L'infection generale a Bacille pyocyanique (Pseudomonas aeruginosa) du nourrisson Semain hop Paris 26 1918 1950

- 96 DECOURT J, SOULLARD J AND CHATEAU R. Méthode a pyocyanique. Traité
ment par la sulfazazine. Guérien. Bulletin m. Soc. m. d. h. ; Paris 61 9
1945
- 97 DE LA CAMP. Zur Kenntnis der Pyocytensepis. Charit. Ann. 3-9^o 1903
- 98 DELATOUR B J. Agranulocytic anemia—A general discussion of the disease
and its treatment. New York J. Med. 3 1 1932.
- 99 DILMOTTE, C. Un cas d'infection pyocyanique causée par le bacille pyocyanique
à l'occlusion staphylococcique. Scalpel 62 139 1910-1911
- 100 DEMUTH W E JR AND RAWSON A J. Pseudomonas septicaemia and endo-
carditis. Am. J. M. Sc. 216 195 1948
- 101 DERBY G S. The Bacillus pyocyaneus found in a case of conjunctitis.
Am. J. Ophth. 2 1 190
- 102 DESBAILLETS P. Un cas d'infection à bacille pyocyanique. Re. med. Suisse
rom. 1 536 19 1
- 103 DITKOWSKI B, GOLDMAN A AND GOLDIN M. Pseudomonas pneumonia in an
infant successfully treated with neomycin. Pediatrics 9 101 1952
- 104 DOLD H. Weitere Mitteilungen über Pyocyaneusinfektion. Arch. f. Sch. f. u.
Trop. n. Hyg. 23 472 1919
- 105 —. Ueber Pyocytensepis und Pyocyaneus-Darmfektion in Shanghai.
Arch. f. Sch. f. u. Tropen Hyg. 27 365 1918
- 106 —. On pyocyanic sepsis and its fatal infection in Shanghai due to
Bacillus pyocyaneus. Ch. e. M. J. 37 435 1918
- 106a DONS N, ERIKSEN K P AND JORGENSEN S. An oxygen therapeutic apparatus
as a source of infection. Ugeskr. laeger 11 1525 1959
- 107 DORLAND W A N. The American Illustrated Medical Dictionary. Ed. III
Philadelphia. W. B. Saunders Co. 1947
- 108 DOUGLAS H, FINEST J AND BETZ H M. Mortality due to pyocyanic infection.
A. m. J. Clin. Med. 7 588 1952
- 109 DUDDEY E. Ueber Ecthyma gangraenatum. Ein Beitrag zu der Pyocyten-
krankung, in der kindlichen Alters. J. h. b. f. k. Kinderh. 99 257 1922.
- 110 EARECKSON V O JR, MILLER J M AND LOCPH H. Infection of the eye
due to Pseudomonas aeruginosa treated with polymyxin B and Vanidol.
A. M. A. Arch. Ophth. 49 158 1953
- 111 EASTMAN J R AND KEENE, T V. Bacillus pyocyaneus pneumonia associated
with blastomycet growth in primary wound. Ann. Surg. 40 613 1904
- 112 EBERT H V AND STEAD E A JR. Circulatory failure in acute infection.
J. Clin. Invest. 9 671 1931
- 113 EHLERS E. To Tilfeld af Ecthyma gangraenatum. Høspital Tidende. Copen-
hagen May 1890
- 114 ELYAN A S. Pyococci pneumoniae a common urinary infection. J. Egypt. An.
Med. 37 724 1954
- 115 EMMERICH R AND LOW O. Bakteriolytische Enzyme als Ursache der
erworbenen Immunität der Heilung. Infektionskrankheiten durch
denselben Zeit. Hyg. 31 1 1899
- 116 ENGLETT F B JR. Spontaneous pseudomonal infection in mice following
injection of milk. Tex. R. p. B. of Med. 12 64 1954

- 117 ENGSTEDT I AND OLTHAGEN B Polymyxinbehandlung *Pseudomonas meningit*
Svenlaktidn 52 196 1955
- 118 ENSIGN P R AND HUNTER C A An epidemic of diarrhea in the newborn
nursery caused by a milkborne epidemic in the community J Pediat
29 620 1916
- 119 EPSTEIN J W AND CROSSMAN A H Bacillus pyocyaneus in children Am J
Dis Child 46 132 1933
- 120 ERNST H C The Bacillus pyocyaneus pericarditis Am J Med Sc 106 395
1893
- 121 ESCHERICH T Pyocyaneu infektionen bei Sauglingen Zentralbl Bakt 23 117
1899
- 122 — Die Verwendung der Pyocyaneu bei der Behandlung der epidemischen
Sauglingsgrippe und der Meningitis cerebrospinalis Wien klin Wchn chr
19 751 1906
- 123 EVANS F Y Primary Meningitis caused by Pseudomonas aeruginosa Bacillus
pyocyaneus A review of the literature and a report of three cases Med Rec
144 111 172 1936
- 124 EVANS F T Septic arthritis in spinal canal Arthritis Proc Roy Soc Med 39 181
1946
- 125 EWELL G H Bacillus pyocyaneus bacteremia secondary to pyelonephritis and
prostatic abscess with death Urol & Cutan Rev 40 697 1936
- 126 FAZEKAS A AND NIKODEMUSZ I Über einen Fall von Pyocyaneu Meningitis
Wien klin Wchn chr 62 903 1950
- 126a FEDORS P Inhibition of Histoplasma capsulatum and Blastomyces dermatitidis
by Pseudomonas aeruginosa in vitro Mycopathologia 11 178 1959
- 127 FEIN B T Bronchial asthma caused by Pseudomonas aeruginosa demonstrated
by bronchoscopic examination Ann Allergy 13 639 1955
- 128 FERGUSON F AND DARR D Glycouria in meningitis Ann Int Med 21 13
1944
- 129 FINKELSTEIN H Bacillus pyocyaneus und hämorrhagische Diathese Charit
Ann 71 316 1896
- 130 FINLAND M Current status of therapy in bacterial endocarditis JAMA
166 364 1958
- 131 FIRKET J AND DOLHA H Infections a Bacillus pyocyanus (Pseudomonas
aeruginosa) pathologie et conditions d'apartenance Re med Liege 8 419
1953
- 132 FISER P E Chronic infective arthritis caused by Pseudomonas pyocyaneus
Canad MAJ 41 515 1947
- 133 FISH G W HAND M D AND KEIM W F JR Acute bacterial endocarditis
due to Pseudomonas aeruginosa (Bacillus pyocyaneus) Am J Path 13 121
1937
- 134 FISHER A M Inhibition of growth of Cryptococcus neoformans by culture
of Pseudomonas aeruginosa Bull Joln Hopkins Hosp 95 157 1954
- 134a FISHER E JR AND ALLEN J H Corneal ulcers produced by cell free
tracts of Pseudomonas aeruginosa Am J Ophth 46 21 1958
- 134b — AND — Mechanism of corneal destruction by pseudomonas protease
Am J Ophth 46 249 1958

- 134c FISHER M W Synergism between human gamma globulin and bl raphenicol in the treatment of experimental bacterial infection Antibiotics & Chemother 7 315 1957
- 135 FLETCHER S The etiology and the classification of pytonitis Philadelphia MJ 1019 1898
- 136 FLOREY H ET AL Antibiotic London Oxford Univ Press 1949 pp 10 et seq
- 137 FLOREY M E, POKS R W, N L, AND TILTON E C Infection of wound with gram negative organism Lancet 1 833 1947
- 138 FLORMAN A L AND SCHIFFER N Observation on a small outbreak of infantile diarrhea associated with Pseudomonas aeruginosa J Pediatr 36 58 1950
- 139 FURDOS M Recherches sur la matiere colorante des suppurations bleues pyocyanine Compt Rend Acad Sc 51 215 1860
- 140 FORKNER C E, JR, FREI E, EDGECOCK J AND UTZ J Pyoclonosis Septicemia (Observation on 23 cases) Am J Med 3 877 1958
- 141 FOTHERGILL, L M AND SWEET L K Measles in infant and children with pyoclonosis J Clin Pathol 1953
- 142 FOX J E AND LOWBURY E J L Immunity to Pyoclonosis pyoclonosis in man J Path & Bact 65 519 1953
- 143 FRADA G Pyoclonosis in pyoclonosis in pyoclonosis Riforma med 61 4 1947
- 144 FRAENKEL E Über die Mechanismenpathogenität des Bacillus pyocyanus Ztchr Hyg 72 486 1912.
- 145 ——— Über Allgemeininfektion durch den Bacillus pyocyanus Virchow Arch path 4 183 405 1906
- 146 ——— Weitere Untersuchungen über die Mechanismenpathogenität des Bacillus pyocyanus Ztsch Hyg 81 369 191
- 147 ——— Ein weiterer Beitrag zur Mechanismenpathogenität des Bacillus pyocyanus Ztchr Hyg 93 135 192
- 148 FREE L C Local infection with the Bacillus pyocyanus Ann Surg 61 19 1916
- 149 FREYSCHMIDT P Die Pyoclonose infektion beim Erwachsenen Arztl Wch 11 10 406 1955
- 150 FRIEDSMANN U Über Angenkrankheiten Med Klin 19 1357 1953
- 151 FRIEDENBERG Z B Obituary with a comment of the hospital J Bone & J Surg Am 37 924 1950
- 152 GABY W L A study of the clinical behavior of Pseudomonas aeruginosa J Bact 51 217 1946
- 153 ——— AND FREE, E Occurrence and clinical significance of non-pigmented strains of Pseudomonas aeruginosa in the clinical laboratory J Infect Dis 63 746 1953 (abstract)
- 154 ——— AND ——— Differential diagnosis of pseudomonas infections in the clinical laboratory J Bact 16 442 1958
- 155 ——— AND HADLEY C Pyoclonosis laboratory test for the identification of Pseudomonas aeruginosa J Bact 4 336 1957

- 155 GAFTHIGENS W. Beitrag zur Bakteriologie der Meningitis. *Zentralbl Bakt* 75 41 1911
- 155a CAILLARD L. DELPHIN D. AND CORNU I. The value of colimycin in the treatment of various Pseudomonas infections. *Pediatr* 14 541 1959
- 156 GAINES S. AND LANDY M. Prevalence of antibody in pseudomonas in normal human sera. *J Bact* 69 628 1955
- 157 GAMBLE M. E. C. AND HARRIS F. C. Pseudomonas pyocyanea simulating enteric fever and developing during antibiotic treatment. *West African MJ* 2 79 19 3
- 158 GARRARD S. D. RICHMOND J. B. AND HIRSCH M. M. Pseudomonas aeruginosa infection as a complication of therapy in pancreatic fibrosis (mucoviscidosis). *Pediatrics* 8 48 1951
- 159 GARRETSON W. T. AND OSCROVE K. W. Ulceration of the cornea due to Bacillus pyocyaneus. *JAMA* 88 90 1927
- 160 GATCHERALD AND PIGEALD H. Meningite a Bacilles pyocyaniques chez un nouveau ne. *Bull Soc l'el'e gynec et ob t* 17 74 1928
- 161 GEPPERT L. J. BAKER H. J. COPPLE H. I. AND PULASKI E. J. Pseudomonas infection in infants and children. *J Pediat* 41 555 1952
- 162 GERMER W. D. AND KNAPP W. Pyocyaneu Meningitis ein Beitrag zur Streptomycintherapie von durch gram negative Bakterien hervorgerufenen Meningitiden. *Med Klin* 44 1591 1949
- 163 GESSARD C. Sur les colorations bleue et verte des langes a pans ments. *Compt rend Acad Sc* 91 536 1882
- 164 — Nouvelles recherches sur le microbe pyocyanique. *Ann Inst Pasteur* 4 III 1890
- 165 — Classement des germes pyocyaniques par les pigments. *Compt rend Soc biol* 82 795 1919
- 166 — Diagnostic pigmentaire du bacille pyocyanique. *Ann Inst Pasteur* 33 911 1919
- 167 — Technique d'identification des germes pyocyanique. *Ann Inst Pasteur* 34 88 1920
- 168 GIEROGHIEWSKY Du mecanisme de l'immunit'e vis a vis du Bacille pyocyanique. *Ann Inst Pasteur* 13 298 1899
- 169 GHON A. Ein Beitrag zur Meningitis durch Bacterium pyocyaneum. *Med Klin* 26 654 1932
- 170 GILBERT R. P. HONIG K. P. GRIFFIN J. A. BECKER P. J. AND ABELSON B. H. Hemodynamics of shock due to infection. *Stanford M Bull* 13 239 1955
- 171 GILL W. D. AND GILL E. K. Otitis externa some comments concerning the present status of therapy. *South MJ* 43 428 1950
- 172 GINSBERG I. A. AND HYMAN G. A. Combined Aureomycin and streptomycin therapy of Pseudomonas aeruginosa (Bacillus pyocyaneus) meningitis with a case report. *Ann Int Med* 37 191 1952
- 173 GIUNCHI G. MARINOZZI V. ORTONA L. AND SORICE F. Politerite e polmonary arteritis caused by Pseudomonas aeruginosa in a case of tetralogy of Fallot. *Minerva med* 48 521 1954

- 174 GLANZMAN E. Zur Klinik der Pyocyaneinfektion im Säuglings- und Kinderalter. *Ann paed* 174 99 1950
- 175 GOLDMAN L. AND FOX H. Greenish pigmentation of nail plates from *Bacillus pyocyaneus* infection: report of 2 cases. *AMA Arch Dermat* 49 136 1944
- 176 GOLDMAN J. L., BLOOM S. M. AND HERCHBERGER C. Bacteriologic and clinical interpretation of the flora of the nose and nasopharynx in children. *J Pediat* 44 299 1954
- 177 GOMES L. DE S., SILVA M. DE B. E. RIBAS J. C. AND CARVALHO L. C. Primary meningitis due to *Pseudomonas aeruginosa* Ca. with relapse followed by recovery: data on frequency of meningitis in São Paulo. *Rev Inst Adolfo Lutz* 10 71 1950
- 178 GORDON A. T. Otitis externa. *Bull US Army Med Dept* 8 215 1948
- 179 GOTTSCHEG G. AND ROMODA T. Subacute bacterial endocarditis caused by *Bacillus pyocyaneus*. *Orv. Hetil* 96 417 1955
- 180 GRABER C. D., TUMBLECH W. T. AND VOGEL E. H. JR. In vitro sensitivity of pseudomonads from burned patient to otitis ulfate. *Antibiotics Annual* 19 9-1960. New York: Antibiotics Inc. 1960 pp 7-9
- 181 GRACEY D. Septicemia of unknown origin. *Brit Med J* 1 904 1930
- 182 GROSSOWITZ N., HAYAT P. AND HALPERN Y. S. Pyocyanine biosynthesis by *Pseudomonas aeruginosa*. *J Gen Microbiol* 16 576 1955
- 183 GROUPE V., PLUGH L. H., WEISS H. AND KOCHI M. Observations on the activity of osin. *Proc Soc Exper Biol & Med* 8 354 1951
- 184 CROVES E. H. A. Incalculable loss of *Bacillus pyocyaneus* pyemia successfully treated by vaccine. *Brit Med J* 1 1169 1909
- 185 GRUBER J. Ueber das Vorkommen grünen Eiters ohne Monstachromophilie. *Zf. Bakt.* 21 145 1887
- 186a GLASSARDO G. La Colimonia in pediatria. *Minerva med* 30 4494 1958
- 186b GLAD D. P. Treatment of corneal infection due to *Bacillus pyocyaneus* with polymyxin B sulfate ointment. *Brit J Ophthalmol* 40 159 1956
- 187 GUY W. H. AND COHEN M. M. Dermatitis exfoliativa neonatorum (Pittier disease). *Arch Dermatol Syph* 19 425 1959
- 188 GYENGES L., BODI T., TOTI L. AND KELEMEN I. Pseudomonas pyocyanine: etiological and epidemiological role of *Pseudomonas pyocyaneus* in diarrhea of premature infant. *Monatsh Kinderheilk* 104 120 1956
- 189 HADLEY P. M. Bacteriostatic activity of bacteriophage with special reference to its dissemination and transmission. *J Infect Dis* 40 1 1957
- 190 HALL W. H. AND GOLD D. Shock associated with bacteremia. *Review of 35 cases*. *AMA Arch Int Med* 96 403 1955
- 191 HAMMOND C. W., RUTLEDGE D., COOPER M. B. AND MILLER C. P. Studies on susceptibility to infection following adaptation. *J Exper Med* 99 411 1954 107 403 1959
- 192 HAND A. M. Pseudomonas aeruginosa sepsis (Pyocyaneus Bacteria) - report and preliminary findings. *South Med J* 4 1049 1951

- 192 HARDY A V MITCHELL R B SCHREINER M ET AL. Laryngoscope 64 1070 1954
- 193 HARRIS C BLUMEN L AND APILEBAUM E. Secondary Bacillus pyocyaneus infection in meningitis following intrathecal penicillin therapy J Lab & Clin Med 31 1113 1946
- 193a HARRIS J R AND SCHICK B. The use of gamma globulin in infection refractory to antibiotic J Mt Sinai Hosp 21 148 1954
- 194 HAYES E R AND LOW E. Meningitis due to Pseudomonas aeruginosa treated with polymyxin I Am J Med 270 633 1950
- 195 HAYNES W C. Pseudomonas aeruginosa—its characterization and identification J Gen Microb 5 939 1951
- 196 HAYS E E WELLS J C KATZMAN P A ET AL. Antibiotic substances produced by Pseudomonas aeruginosa J Biol Chem 159 725 1945
- 197 HAZEN H H. A case of pemphigus foliaceus J Cutan Dis Incl Syph 28 118 1910
- 198 HEINECKER R. Beitrag zur antibiotischen Behandlung der Pyocyaneus-Meningitis (Pseudomonas meningitis) Arzt Forsch 7 65 1953
- 199 HENSON S W JR AND COVENTRY M B. Osteomyelitis of the vertebrae as the result of infection of the urinary tract Surg Gynec & Obst 107 90 1956
- 200 HERRILL W E AND NICHOLS D R. The clinical use of streptomycin—a study of 45 cases Proc Staff Meet Mayo Clin 20 449 1945
- 201 HERTZOG A J. A study of 317 cases of fatal meningitis with special reference to bacteriologic diagnosis Am J Clin Path 15 571 1945
- 202 HILLS H F. Case of puerperal septicemia due to Pseudomonas aeruginosa with a short review of the literature J Obst & Gynec Brit Emp 56 860 1949
- 203 HIRSCHBERG M. Akute Orchitis durch Pyocyaneus infektion Deutsche med Wchnchr 33 1787 1907
- 204 HIRSZFELD H, KALSKI A MOSZKOWSKA I SKORSKA S AND BEKORAUAST A. L'infection du nourrisson par le bacille pyocyanique Arch franç pediat 5 565 1948
- 205 HITSCHMANN R AND AREIBICH K. Zur Pathogenese des Bacillus pyocyaneus und zur Aetiologie des Ekthyma gangrenosum Wien klin Wchnchr 10 1093 1897
- 206 HOBBS M L HARLEY J B AND LOVE H E. Meningitis due to Pseudomonas aeruginosa following myelography with pantopaque West Virginia MJ 53 180 1957
- 206a HOEKENGA M T CARRIZO H AND GREEN W E. Treatment of severe infectious diarrhea in infants with colistin salts Antib Med & Clin Therapy 7 314 1960
- 207 HOFFMAN M A AND FINBERG C L. Pseudomonas infections in infants associated with high humidity environments J Pediat 46 626 1955
- 208 HOFMANN H U. Pyocyaneus—Sepsis bei einem neugeborenen Zwilling kind intrauterine oder früh-postnatale Schädigung Kinderarztl Praxis 27 453 1954
- 209 HOLGATE J. A fatal case of pseudomonas infection West African MJ 3 145 1954

- 210 HOPPER J JR JAWETZ E AND HINMAN F JR Polymyxin B in chronic pyelonephritis. Observation on the safety of the drug and its influence on renal function. *Am J Med Sc* 25:40 1953
- 211 HORDER T S A case of pyocyanaemia following otitis media. *Bacillus pyocyaneus meningitis of otitic origin*. Tr Path Soc London 55:140 1904
- 212 HOSoya S HOMMA Y ECAMI F AND YAGI Y On the isolation of antigenic substances from *Pseudomonas aeruginosa* in a Japanese. *J Exper Med* 20:55 1919
- 213 HOWE C W Invasive infections due to the genus *Pseudomonas*. *Surgery* 29:48 1951
- 214 HUBBARD J D KING H AND BEAHER I R The pathogenicity of *Pseudomonas aeruginosa* (Bacillus pyocyaneus). Experimental studies and report of a case. *Am J Clin Path* 28:43 1957
- 215 HUBNER E n Fall n Pyocyaneus epi-leim Erwachsene. *Deutsche Medizinische Wochenschr* 33:803 1907
- 216 HUGHES G C AND KIRBYAN H A A report of *Pseudomonas aeruginosa* active in vitro against *M. tuberculosis*. *Nature Lond* 159:197 1947
- 217 HUNTER C AND ENSIGN J An epidemic of diarrhoea in a newborn nursery caused by *Pseudomonas aeruginosa*. *Am J Pub Health* 37:1166 1947
- 218 HYMAN A AND EDELMAN L Medical and urological aspects of bacterial infection in urology. *J Urol* 78:113 1952
- 219 IBRAHIM A P A case of traumatic epistemic meningitis caused by *Bacillus pyocyaneus*. *J Egyptian Med Ass* 20:599 1953
- 220 IWASAKI S AND MOTINAGA H Ein Fall n Pyocyaneus-Meningitis nach Pneumonie. *ephalologische Oky mlgkkt 7a h 51* 11/80 1939
- 221 JACKSON D M LOWBURY E J L AND TOLLEY E Pseudomonas pyocyaneus in turn of as a pathogen in the skin of locusts. *Polymyxin therapy*. *Lancet* 2:137 1951
- 222 JACOB F Biographie in luitte et mode d'action d'une pyocine antibiotique. *Pseudomonas pyocyaneus*. *Ann Int Pte r* 86:149 1954
- 223 JACOBI P Ueber einem Fall. *Ulrichs Annalen* gerufen durch den *Bacillus pyocyaneus*. Theil Heidelberg G. Geier 1912
- 224 JADAWITSCH W A Zur Lehre von der Pathogenität des *Bacillus pyocyaneus*. *Medicinalische Beobachtungsmittel n Jahre Zeitschrift* 1890 Bd 31: 992 et
- 225 JANSSE B Meningitis Due to *Pseudomonas aeruginosa* (Bacillus pyocyaneus). *Maandblad der Geneesk* 2:367 1954
- 226 JAWETZ E Infection with *Pseudomonas aeruginosa* treated with polymyxin B. *AMA Arch Int Med* 89:90 1952
- 226a — Polymyxin B. *Ed H Welch New York Medical Encyclopaedia* 1956 pp 11-35
- 227 JONES R F M A case of Pseudomonas pyocyaneus meningitis of otitic origin treated with polymyxin. *J Laryng & Otol* 69:561 1953
- 228 JORDA E O Bacillus pyocyaneus and its pigment. *J Exper Med* 4:627 1899
- 229 JOY H H Treatment of epithelial Bacillus pyocyaneus ulcer of the cornea with hydroxybutyric acid. *AMA Arch Ophth* 27:1135 1942
- 230 JUSTI K Ueber Pyocyaneus kulturen in den *Indere des Darm*. *Arch Schiffs- u Tropenhyg* 19:458 1915

- 192 HARDY A V MITCHELL, R B., SCHREIBER, M., ET AL. Laryngo cope III 10 0 1954
- 193 HARRIS C BUXBAUM L AND APPLEBAUM E. Secondary Bacillus pyocyaneus infection in meningitis following intrathecal penicillin therapy J Lab & Clin Med 31 1113 1946
- 193a HARRIS J H AND SCHICK H. The use of gamma globulin in infection refractory to antibiotic J Mt Sinai Ho 21 148 1954
- 194 HAYES E P AND YOW E. Meningitis due to Pseudomonas aeruginosa treated with polymyxin B Am J Med 20 633 1950
- 195 HAYNES W C. Pseudomonas aeruginosa—its characterization and identification J Gen Microb 5 939 1951
- 196 HAYS E E, WELLS I C, KATZWAN P A, ET AL. Antibiotic substances produced by Pseudomonas aeruginosa J Biol Chem 159 725 1945
- 197 HAZEN H H. A case of pemphigus foliaceus J Cutan Dis incl Syph 28 118 1910
- 198 HEINECKER R. Beitrag zur antibiotischen Behandlung der Pyocyaneus—Meningitis (Pseudomonas meningitis) Arztl Forch 7 65 1953
- 199 HENSON S W JR AND COVENTRY M B. Osteomyelitis of the vertebrae as the result of infection of the urinary tract Surg Gynec & Obst 107 707 1956
- 200 HERRELL, W E AND NICHOLS H R. The clinical use of streptomycin—a study of 45 cases Proc Staff Meet Mayo Clin 20 449 1945
- 201 HERTZOG A J. A study of 377 cases of fatal meningitis with special reference to bacteriologic diagnosis Am J Clin Path 15 51 1945
- 202 HILLS H F. Cases of puerperal ptychicemia due to Pseudomonas aeruginosa with a short review of the literature J Obst & Gynec Brit Emp 56 860 1949
- 203 HIRSCHBERG M. Akute Orchitis durch Pyocyaneusinfektion Deutsche med Wchnchr 33 1782 1907
- 204 HIRSZFELD H, KALSKI A, MOSZKOWSKA I, SKORSKA S AND DEKORUNST A. L'infection du nourrisson par le bacille pyocyanique Arch franç pediat 5 565 1948
- 205 HITSCHMANN H AND KREIBICH K. Zur Pathogenese des Bacillus pyocyaneus und zur Aetiologie des Ekthyma gangrenosum Wien klin Wchnchr 10 1093 1897
- 206 HOBBS M L, HARLEY J B AND LOVE H E. Meningitis due to Pseudomonas aeruginosa following myelography with pantopaque West Virginia MJ 53 180 1957
- 206a HOENENGA M T, CARRIZO H AND CREEV W H. Treatment of enteric infectious diarrhea in infants with coltin salts Antib Med 3 Clin Therapy 7 314 1960
- 207 HOFFMAN M A AND FINKEL C L. Pseudomonas infections in infants associated with high humidity environment J Ped 146 66 1955
- 208 HOFMANN H U. Pyocyaneus—Sepsis bei einem neugeborenen Zwilling kind intrauterine oder früh-postnatale Schädigung Kinderarztl Praxis 2 453 1954
- 209 HOLGATE J. A fatal case of Pseudomonas infection West African MJ 3 145 1951

- 19 KRACKE, H. H. AND PARKER F. Etiology of granulopenia (agranulocytosis) with particular reference to drugs containing benzene ring. *J Lab & Clin Med* 19 99 1931
- 20 KRAFT C. L. Experimentel pathologische Studien über akute Peritonitis. Copenhagen: Langsted, 1891
- 21 KRANHALS H. Ueber Pyocyaneinfektionen. *Deutsch. Zeitschr. Chir.* 3 181 1893
- 22 KRAUS E. J. AND HUNTER M. P. Congenital facillus pyocyanus infections. *Am. Arch. Path.* 31 819 1911
- 23 KREITNER H. Die Pyocyaneinfektion und ihre Behandlung. *Wien. klin. Wochenschr.* 64 369 1922
- 24 KREMER M. Meningitis after spinal anesthesia. *Brit. M. J.* 2 309 1945
- 25 KREPLER Pyocyane Osteomyelitis der Wirbelsäule bei einem Säugling mit Pyocaneum nekrose. *Monatsschr. Kinderh.* 107 161 1954
- 26 KRETCHMER H. L. AND OCKLEY E. A. Osteomyelitis secondary to infection of the genitourinary tract. *J. Urol.* 34 117 1935
- 27 KRIEGER W. AND PAQUALE A. Untersuchungen über Dysenterie und Leberabscesse. *Zeitschr. Hyg.* 16 1 1894
- 28 KUSONOKI, T. A case of Pseudomonas osteomyelitis of the spinal column in connection with pyelonephritis. *Zeitschr. Urol.* 137 619 1938
- 29 LACRIFOUL, A., BOLSQUET A. D. ROGER H. La typhophocyan (pyocyanine) éralisée à forme typhoïde. *Comptes Rendus Acad. Sci.* 68 1019 1910
- 30 LANE, E. H. AND CHURCH C. H. C. Pubic and ischial necrosis following cytometry and prostatectomy (Osteitis pubis). *Am. J. Roentgenol.* 1 193 1934
- 31 LANE E. L. Arthritis of hip following urinary tract infection. *Radiology* 65 194 1955
- 32 ——— Vertebral osteomyelitis following urinary tract operation. *Am. J. Roentgenol.* 59 38 1956
- 33 LANDY M. JOHNSON A. G. WEBSTER M. E. AND SAGIN J. F. Studies in the O antigen of *Shigella* typhi. *J. Imm.* 74 466 1955
- 34 LARTAUD A. J. A contribution to the study of the pathogenesis of the Bacillus pyocyanus with special reference to its relation to the production of dysentery. *J. Exptl. Med.* 3 59 1898
- 35 ——— The Bacillus pyocyanus in the etiology of human pathology with the report of three cases. *Philadelph. M. J.* 2 562 1898
- 36 LAZARUS J. A. AND SCHWARZ L. H. Septic therapy in Pseudomonas aeruginosa infections of the urogenital tract with specific reference to the urological tract. *Urol. & Cutan. R.* 57 65 1948
- 37 ——— AND ——— Unusual strain of Pseudomonas aeruginosa associated with the urinary bladder. *Am. J. Med. Sci.* 16 1948
- 38 LEACHMAN H. S. Toxic nephritis in Bacillus pyocyanus septicemia. *M. J. & Re.* 131 57 1930
- 39 LEIGH T. F. KELLY R. I. AND WEXES H. S. Spinal osteomyelitis associated with urinary tract infection. *Radiology* 63 331 1955
- 40 LEVINEBERG H. Etiologie des pyocyanischen septischen Knochentumors. *No. d. med. W.* 12 389 1941
- 41 LEONE H. Contributo alla conoscenza della malattia polmonare e

- 231 KAILAN H S, SPECK R S AND JAWETZ E. Impairment of antimicrobial defense following total body irradiation of mice. *J Lab & Clin Med* 40 687 1952
- 232 KEARN J J. Malignant endocarditis due to *Bacillus pyocyaneus*. *AMA Arch Path* 21 839 1936
- 233 KEEFER C S AND HEWITT W L. The therapeutic value of streptomycin in 3000 cases. Ann Arbor Mich. J W Edwards 1948
- 234 KEENEY M J. Pyocyanic angina with agranulocytosis. Report of case. *California & West Med* 33 502 1930
- 235 KENOYER W L, STONE, C T AND LEVIN W C. Bacterial endocarditis due to *Pseudomonas aeruginosa* treated with neomycin. *Am J Med* 13 108 1952
- 235a KEOWN K K, GILMAN H A AND BAILEY C P. Open heart surgery: anesthesia and surgical experiences. *JAMA* 165 781 1957
- 236 KERBY G P. *Pseudomonas aeruginosa* bacteremia with report of a case. *Am J Dis Child* 74 610 1947
- 237 KERNAN W Z, PERLSTEIN M A AND LEVINSON A. *Bacillus pyocyaneus* meningitis following pneumoencephalography. *Am J Dis Child* 63 912 1943
- 238 KIERLAND R R AND KULWIN M H. Clinical evaluation of a new pyrogenic agent. *Arch Dermat & Syph* 62 571 1950
- 239 KIRZ E. Osteitis pubis after suprapubic operation on the bladder with report of 10 cases. *Brit J Surg* 34 272 1947
- 240 KLIEWE H AND KOCH. *Pyocyaneus meningitis*. *Munchen med Wchn chr* 71 867 1924
- 241 KLINE H S AND MASCHKE A S. Three fatal cases of *Bacillus pyocyaneus* infection. *JAMA* 93 528 1937
- 242 KNIGHT V, HARDY R C AND NEGRI J. Meningitis due to *Pseudomonas aeruginosa* treated with streptokinase and streptodornase and intramuscular and intrathecal treatment with neomycin. *JAMA* 149 1395 1942
- 243 KOCH M L. Bacteremia due to bacterial species of the genus *Aerobacter*. *Escherichia Pseudomona*. *Antibiotic med* 9 113 1956
- 243a KOHLENBRENER R M, BOEHM J J AND FALK A H. *Pyoderma gangrenosum* pseudomonas infection versus the Schwartzman phenomenon. *AMA Am J Dis Child* 96 741 1958
- 244 KOHN W. Fatal Candidiasis and *Pseudomonas aeruginosa* septicemia in a fetus as a result of antibiotic therapy. *Maryland MJ* 6 254 1957
- 245 KOPETSKY S S AND ALMOUR, H. Erysipelas following *Bacillus pyocyaneus* infections in mastoid wounds. *Am J Surg* 2 589 1927
- 246 KORLOF H. Different methods of treating pseudomonas infected burns. *Acta chir Scandinav* 107 244 1954
- 247 KORTE W. *Pyocyaneus* Infektion beim Neugeborenen intruterin erworben. *Pyocyaneus* infections of the newborn acquired in the uterus. *Zchr Geburtsh* 144 291 1955
- 248 KOSEL, H. Zur Fixation der Pathogenität des *Bacillus pyocyaneus* für den Menschen. *Zchr Hyg* 16 368 1893
- 248a KOYAMA Y, KUROSAWA A, TSUCHIDA A AND TAKAKUTA K. A new antibiotic colistin produced by spore forming soil bacteria. *J Antib* 3 457 1950

- 293 MANAS M A Lung disease induced by *Pseudomonas aeruginosa* Rev med cubana 6 1 1956
- 294 MANOUKIAN M Otitis pubis due to *Pseudomonas aeruginosa* treated with polymyxin B sulfate JAMA Arch Ophth 73 1953
- 295 MARKLEY K GURMEZI C CHAVEZ P M AND BAZAN A Fatal pseudomonas septicemia in burn patients Ann Surg 137 1 1953
- 296 MARSH H F STENGEL H H AND STEW J M An unusual strain of *Pseudomonas aeruginosa* Am J Dis Child 8 1952 1959
- 297 MARTSEN G Medizinische Deklaration der Friedrich-Wilhelms-Universität zu Berlin (1890) Quoted by Lazarus J A New York J Med 6 1/2 1957
- 298 MARTIN W J PITTELL J A JR WILLIAMS W H AND CERACE J E Bacteremia owing to pseudomonas—Review of 10 cases Proc Staff Meet Mayo Clin 79 1954 1955
- 299 MASI A AND DETTORI M A case of meningitis *Pseudomonas* 281 1953
- 300 MAYR HARTING A The ecology of *Pseudomonas pyocyanea* J Gen Microb 2 31 1948
- 300a M CARL W R JACKSON C AND HENRY V M Clinical and laboratory bacteriology in the use of tin in infections by gram negative bacilli Ann Int Annual 19 9 1960 New York, Antistat Assoc 1960 pp 80-88
- 300b MCCARTNEY E T AND STEWART J Suppurative orchitis due to *Pseudomonas aeruginosa* J Pediatr 52 1957
- 301 MCCORDY R S AND NEYER E Effect of penicillin on the spectrum and biologic properties of a gram negative bacterium flora in the upper respiratory tract of infant Pediatr 9 2 1957
- 301a M D VALD L W RHOADS J S AND KAYE A B Bacterial endocarditis due to *Pseudomonas aeruginosa* JAMA 16 1490 1958
- 302 MCFARLANE A M (ROSE) B AND TEE C H Variation in bacteriology of the throat in the infant in the maternity unit Brit Med J 2 1140 1949
- 303 McLEOD J W The hospital as a host and bed of a reservoir of infection by *Pseudomonas pyocyanea* Lancet 1 394 1958
- 304 MEDICOLE et (PORTSMOUTH CASE) Meningitis following spinal anesthesia. Brit Med J 1 660 194
- 304 ——— Meningitis following spinal anesthesia Brit Med J 1 44 1948
- 305 MELINA F Sulfonamide resistance in *Pseudomonas aeruginosa* Ho piociano nell uomo Ridher 2 43 1946
- 306 MELTZER S J Lieberstein Methode der experimentellen Erzeugung von Pseudomonas ulcerae percutanea Methode der Ergebnisse Berl Klin Wochenschr 131 1914
- 307 MERWARTH H P ROEYER M AND ILLIOTT F *Pseudomonas* meningitis followed by unusual complications attributed to treatment with streptomycin Boklyn Hosp J 5 93 1947
- 308 MEYER M F AND RUSSELL J C Ocular abscess (following foreign body in eye) and meningitis with recovery JAMA Arch Ophth 73 415 1955
- 308a MEYER I O *Pseudomonas aeruginosa* as a cause of necrotizing renal pyelitis case report Am J Obstet Gynec 19 168 1960

- cutanea progressiva da piociano ad e isto montale Minerva dermat 29 297 1954
- 272 LEIARD C W B Pyocyanus ulcer Report of three cases results of sulfa pyridine therapy in one case A M A Arch Ophth 28 180 1949
- 273 LESLIE N Correlation of clinical otitis externa with mycolacteriologic studies A M A Arch Otolaryng 58 716 1953
- 274 LEVADITI J C Mise en evidence a l'aide d la microscopie en ultraviolet de la fluorescence bacterienne primaire ou propre Compt rend Soc biol 137 318 1943
- 275 LEVY J I AND COHEN A E Pyocyanus meningitis after lumbar puncture Report of a case with apparent recovery J A M A 85 1968 1925
- 276 LEWIN W Gram negative meningitis following head wound with special reference to infection with coliform bacilli Brit J Surg 35 266 1948
- 277 — AND VOLLM P L Streptomycin treatment of meningitis due to gram negative saprophyte Lancet 2 416 1948
- 278 LIEBERG N C F AND ARTZ C P Infection in burns III Septicemia a common cause of death Surg Gynec & Obst 99 151 1954
- 279 LILLEY A B AND BEARLE A J Generalized infections due to Pseudomonas aeruginosa (Bacillus pyocyanus) with study of characteristics of local strain of organism M J Australia 1 362 1928
- 280 LINDSAY J W RICE E C AND SELINGER M A The treatment of meningitis due to Hemophilus influenzae (Pfeiffer's bacillus) A review of 108 cases J Pediat 17 290 1940
- 281 LINTHICUM F H Experimental work with the Bacillus pyocyanus tomatis with aggranulocytic leukopenia Ann Otol Rhinol & Laryn 36 1093 1927
- 282 LODENKAMPER H AND SCHIEBERMANN O Über Pyocyanus Meningitis Ztschr klin Med 146 147 1950
- 283 LOHLEIN W Experimentelle Untersuchungen zur Keratitisfrage Arch f Augenh 96 265 1925
- 284 LOVELL SMITH H D Meningitis due to pseudomonas treated with polymyxin B New Zealand M J 53 520 1954
- 285 LOVETT B R Aggranulocytic anemia J A M A 83 1498 1924
- 286 LOWBURY E J L Contamination of cetrimide and other fluid with Pseudomonas pyocyanus Brit J Indust Med 8 22 1951-1952
- 287 — AND FOX J Epidemiology of infection with Pseudomonas pyocyanus in a burn unit J Hyg 52 403 1944
- 288 LUCHE A De oenanthe blau Eiterung und ihre Ursachen Arch klin Chir 3 135 1862
- 289 MABILLE BERVES AND COCHIVARD Un cas de meningite a B Pyocyanique traite par la polymyxine B Tunis med 43 159 1948
- 290 MACDONALD M Pseudomonas pyocyanus eye infection Brit J Ophth 37 370 1953
- 291 MACKENZIE P A H Bacillus pyocyanus in the blood stream in a case of aggranulocytic anemia Canad M A J 24 471 1931
- 292 MALLANAH S Infection by Bacillus pyocyanus simulans, letro y Brit M J 2 1223 1922

3. NISSEY N M, McLELLAN J, ANTHONY J J AND GINGER L C. Bacterial pyrogen in tyrocin preparation from a *Pseudomonas* species. *J Am Pharm Assoc (Sci Ed)* 39:456 1950
34. JETER E, KUNZ E H AND MORGAN E H. Synergistic effects of polymyxin B and Terramycin on bacteria encountered in urinary tract infection. *J Urol* 64: 3 1950
35. ———, KRAUS R F, EGAN G J AND MASON T H. Aureomycin Treatment of meningitis due to *Bacillus pyocyaneus* and *Bacillus aerogenes*. *JAMA* 147:133 1950
36. ——— AND WEINSTEIN D H. Epidemiological study on *Pseudomonas aeruginosa* (*Bacillus pyocyaneus*) in premature infant in the presence and absence of infection. *J Pediatr* 46:20 1955
37. NEWTON B A. Site of action of polymyxin on *Pseudomonas aeruginosa* antagonism by cation. *J Gen Microbiol* 10:491 1954
38. ———. The action of polymyxin on *Pseudomonas pyocyanea*. *J Gen Microbiol* 8:Proc vi 1953
39. ———. Relation of the antibacterial activity of polymyxin by dialysis. *Nature London* 17:160 1953
40. ———. Release of soluble constituent from washed cell of *Pseudomonas aeruginosa* by the action of polymyxin. *J Gen Microbiol* 9:14 1953
41. NICOLA G AND SAVINA A. Resistenza *Pseudomonas pyocyanea* in galassali e mense con esito negativo a riscontro del galassale nel feto e nel liquido amniotico. *Clin Obstet* 54:306 19
42. NIKHIL CHANDRAN. Systemic infection with *Bacillus pyocyaneus*. Review of literature and report of seven cases. *Chinese MJ* 50:151 1936
43. O'BRIEN J R. Fatal bronchitis-hebbronchitis due to *Pseudomonas pyocyanea* in two siblings. *Lancet* 1:69 1950
44. OETTINGER. Un cas de maladie pyocyaneuse chez l'homme. *Semin med* 10:385 1890
45. OLIVAKY L. Mucin as a resistance lowering substance. *Bact Rev* 12:149 1948
46. ———, AVITERY S AND KORN P A. The hypothermic and adrenergic effect of bacterial vaccine. *J Immunol* 45:37 1947
47. OLSEN W. *Molecular and clinical theory and practice*. Ed. 3. W. O. Le and T. McCrea. Philadelphia and New York: Lea Brothers & Co. 1950 Vol 1:536
48. PAGE I H AND TAYLOR R D. Pyrogenesis in the treatment of malignant hypertension. *Mod Concept Cardiovasc Dis* 18:51 1949
49. PAINTE T F, MURRAY B, SEELEN A O AND FINLAND M. Streptomycin in the treatment of meningitis—Report of twenty-seven cases treated at the Boston City Hospital. *Ann Int Med* 27:493 1947
50. PASTOR B H, GERTER W I AND BARK S. *Pseudomonas aeruginosa* meningitis following spinal anesthesia. Report of two successfully treated cases. *Ann Int Med* 7:1137 1951
51. PAWLOWSKI A D. *Ann Int Med* 35:1 1889
52. PENDEXTER, S E. In *Pyocyanin* neonatal treated with penicillin. *Am J Ophthalm* 31:862 1948

- 309 MILLER C P HAMMOND C W AND TOMKINS M The incidence of bacteremia in mice subjected to total body X irradiation *Science* 111 510 1950
- 309a MILLICAN H C RUST J AND ROSENTHAL S M Gamma globulin factors protective against infections from pseudomonas and other organisms *Science* 126 509 1957
- 309b — — — VERDER E AND ROSENTHAL S M Experimental chemotherapy of pseudomonas infections I Production of fatal infections in cortisone treated mice *Antibiotics Annual 1956 1957* New York Medical Encyclopedia Inc 1960 pp 486-493
- 310 MILLS G Y AND KAGAN B M Effect of oral polymyxin B on *Pseudomonas aeruginosa* in the gastrointestinal tract *Am Int Med* 40 26 1951
- 311 MILLER A MACLEAN H AND MCELWAIN N Treatment of intestinal infections associated with low grade pathogenic bacteria *Rev Gastroenterol* 19 122 1952
- 312 MIRABELL E *Bacillus pyocyaneus* septicemia in infancy and childhood experiences at San Juan City Hospital Bol Asoc med Puerto Rico 41 89 1952
- 313 MITSUI Y AND HANABUSA J Corneal infections after cortisone therapy *Br J Ophth* 39 244 1955
- 314 MONNET P AND BIGUET MERMET G Surinfection meningee par induration au cours de explorations et therapeutique rachidiennes medicales *Bull med Paris* 67 243 1953
- 315 MONNIER Bronchopneumonie et pyohemies a streptocoques et a bacille pyocyanique *Gaz med de Nantes* 12 42 1893
- 316 MOORE M AND MARCUS M D Green nails—The role of *Candida* and *Pseudomonas aeruginosa* *AMA Arch Dermat* 64 499 1951
- 317 MOORMAN L T AND HERBERT F Treatment of pseudomonas corneal ulcers *AMA Arch Ophth* 53 345 1955
- 318 MORAGLES V AND NADERSON W A D Endocarditis due to *Pseudomonas aeruginosa* *Ann Int M* 19 146 1913
- 319 MOREAU H CLER H NATIVELLE H ETIENNE Septicemie a *Pseudomonas aeruginosa* (bacille pyocyanique) revelee par une agranulocytose et terminee par une leucemie maligne [Septicemia followed by malignant leukemia (leukemia)] *Bullet mem Soc med hop Paris* 6 705 1951
- 320 MUNOZ J SCHERAGO M AND WEAVER H H A serological study of members of the *Pseudomonas* genus *J Bact* 57 269 1919
- 321 MUNROX D S AND COCKCROFT W H Septicemia due to gram negative bacilli *Canad MAJ* 72 586 1955
- 322 NEAL J B Meningitis Distribution according to age and etiology *JAMA* 89 1429 1924
- 323 — — — Meningococcal meningitis in children *JAMA* 105 568 1935
- 323a NELSON E L AND BECKER J R The effect of whole body x irradiation on the bactericidal activity of phagocytic cells *J Infect Dis* 101 13 19 9
- 323b — — — AND — — — Survival of *Pseudomonas aeruginosa* within liver and spleen of mice *J Infect Dis* 101 20 1959
- 324 NEMES M M The influence of the B group of vitamins on the production of pyocyanin growth and virulence of *Pseudomonas aeruginosa* *II* *Abstracts* 13 635 1953

- 335 REITTER H Die Iyosaneus Meningitis nach Lumbalpunktion Zentralbl. Chir 16 181 1931
- 336 RHODES P S The clinical analysis of 550 cases of bacterial meningitis. Diagnostic features and various method of treatment Am Practitioner 2496 1933
- 337 — HAYNE A L, IEVIN B ET AL The treatment of pneumococcal meningitis JAMA 115 917 1940
- 338 RINGEN L M AND DRAKE, C. H Studies of the incidence of Pseudomonas aeruginosa in various natural sources J Bact 64 841 1952
- 339 ROBERTS J M H AND BELSEY R Acute Bacillus pyocyaneus meningitis spontaneous recovery Br Med J 2 1276 1937
- 340 ROBINSON S S Septicæmia eruptions—with special reference to the differential effect of a potent drug eruption Urol & Cutan Rev 41 420 1937
- 341 ROBITZEK E H AND PRALSNITZ G Infection with the Bacillus pyocyaneus (Pseudomonas aeruginosa) Review of literature and case report Quart Bull Sea View H 8 21 1946
- 342 ROSSON J H AND SCOTT C I Local treatment of a perimetritic Bacillus pyocyaneus ulcer of the cornea with Albucid Soluble Nature London 148 16 1941
- 343 ROLLY Pyocyaneus epibacterium n. sp. Munhenchener Wochenschr 53 1399 1906
- 343a ROSENTHAL, S M MILLICAN R C AND RIST J A factor in human gamma globulin preparation active against Pseudomonas aeruginosa infection Proc Soc Exper Biol & Med 94 214 1957
- 344 ROSS J Polymyxin in experimental ocular Pseudomonas aeruginosa infection Am J Ophth 35 1952
- 344a PONS S, PLIC J P AND ZAREMBA E A Colistin hemipolymers in laboratory and clinical observation in specific atonenteritis infant and children Abstracts Annual 1959 1960 New York, Antibiotic Inc 1960 pp 89 100
- 345 PLUMPTRE T D Bacteriophage Typhoid bacillus and its detection in culture of Bacillus pyocyaneus Dtsch med Wochenschr 19 987 1893
- 346 SARANT, C Ulcer of the cornea caused by Bacillus pyocyaneus and its treatment JAMA 34 4 1910
- 347 SALVIN S B AND LEWIS M L Extinction of Bacillus pyocyaneus in the guinea pig J Path & Bact 51 49 1916
- 348 SANDIFORD P H Observations on Pseudomonas pyocyaneus J Path & Bact 44 567 1937
- 349 SATTLER H Die Bacillen der Phthalmitis Bericht Ve amnulo g Ophth Gellch He d lb rg 1 201 1891
- 350 SCHAEFER A J AND OPPENHEIM E H Pseudomonas (pyocyaneus) infection of the conjunctival tract in infant children South Med J 41 460 1948
- 351 SCHENK A J Bacillus pyocyaneus and myli of the eye Report of a successful treatment with sulfanilamide AMA Arch Surg 41 40 1910

- 339a PENNISI J A LAWRENCE G J JR AND VEPROVSKY E C Bacteremic shock associated with pseudomonas septicaemia and stillbirth Am J Obst & Gynec 16 1294 1958
- 340 PERKINS R G Report of nine cases of infection with Bacillus pyocyaneus J Boston Soc Med Sc (J Med Res) 8 281 1901
- 341 PESINA M AND HONL J Quoted by Evans F L Beitrag zur Kenntnis der assoziativen Wirkung der Bakterien Internat klin Pündschau 8 1753 1894
- 342 PETERSON U K SCHAEFER H AND WARNECKE H Die antibiotische Behandlung der Pyocyaneusmeningitis Ztschr Kinderh 73 396 1953
- 343 PIETTE J Sur un cas de Meningite a Pyocyaneus Union med Canada 82 895 1953
- 343a PILLEMER L BLUM L LEPOW I H ROSS O A TODD E W AND WARDLAW A C The properdin system and immunity I Demonstration and isolation of new serum protein properdin and its role in immune phenomena Science 170 279 1954
- 344 PINELLI A Artrite monoarticolare primitiva da piociano in una lattante di 8 mesi Pediatra 35 147 1957
- 345 PINGHUI V LIU Survey of hemolysin production among species of pseudomonads J Bact 14 718 1957
- 345a PLOTKIN S A AND AUSTRIAN H Bacteremia caused by pseudomonas species following the use of materials stored in solution of a cationic surface active agent A J M Sc 235 621 1958
- 346 POTE W W H AND COLVILLE C H Intracranial complications of infection of the nasal air passage and accessory sinuses A further report on the nature and incidence of lesions observed in a series of 30 000 autopsies Bull Los Angeles Neurol Soc 10 114 1945
- 347 PROPPE A Aureomycin Heilung einer pemphigoiden Pyocyaneus Septis (Aureomycin treatment of pemphigoid pyocyaneus septicaemia) Hautarzt 3 494 1952
- 348 PULASKI H J AND MATHEWS C S Streptomycin in surgical infection III Otitis externa otitis media mastoiditis brain abscess and meningitis A M A Arch Otolaryng 43 503 1947
- 349 PYRAH L N GOLDIE W PARSONS F M AND RAPER F P Control of pseudomonas infection in a urology ward Lancet 269 314 1955
- 350 PADATS Sur une nouvelle race du bacille pyocyaneus Compt rend Soc biol 4 808 1897
- 351 RADKE R A AND CUNNINGHAM G C A case of meningitis due to Pseudomonas aeruginosa (Bacillus pyocyaneus) and Neisseria flavescens with recovery J Pediat 33 99 1949
- 352 RAIM N C E RAIM J AND LYTTON L Abcess of the epiglottis J A M A 159 1289 1955
- 353 REICHEL H Über Allgemeininfektion mit Pyocyaneusbazillen Deut Arch klin Med 171 299 1931
- 354 REICHMANN F J REYNOLDS G E JR AND MARSH H F Pseudomonas infection of the mandible with discussion and case report South Surgeon 15 606 1949

- 91 SINGER D E, FREEMAN F, HOFFERT W H ET AL. Otitis externa Bacteriological and mycological study. *Ann Otol Rhinol & Laryng* 61 317 1952
- 392 SLITSKY N AND MATLIN I. Pyocyanus in its Role of the larynx and report of an original case. *JAMA* 113 1100 1939
- 393 SMITH C E. C. *Cl. ulimona* meningitis treated with chloromycin and streptomycin. *MJ Malaya* 30 1953
- 394 SMITH E S. Pseudomonas in its infants and children a review of 409 cases. *J Pediatr* 4 425 1954
- 395 SMITH R T. Septicemia and Meningitis in a newborn infant Simultaneous infection with *E. coli* and *Pseudomonas aeruginosa* with recovery. *J Pediatr* 4 140 1955
- 396 SOBHI H AND KHAIRAT O. Intrauterine septicemia due to *Pseudomonas pyocyanus*. Failure with streptomycin. *Brit MJ* 2 516 1948
- 397 SOIFER J D. *Bacillus pyocyaneus* septicemia of placental origin. *Am J Obst & Gynec* 16 889 1928
- 398 SOLTMAN C. Zur Lehre von der Pathogenität des *Bacillus pyocyaneus*. *Deutsche Arch klin Med* 73 600 1907
- 399 SORENSCHNIG C. Die Mucos-Formen des *Pyocyanus*—Lakterium *Bakterium pyocyaneum mucosum*. *Zentralbl Bakt I Abt Orig* 104 365 1927
- 400 —. Todliche Meningitis bei Inhalation. *Deutsche med Wchnsch* 49 881 1923
- 401 SORSEY A AND BIRN H A. Treatment of infected corneal ulcers by subconjunctival injection of penicillin in doses of 1 million units. *Brit J Ophthalm* 11 16 1950
- 402 SPENCER W H. *Pseudomonas aeruginosa* infection of the eye. *California Med* 9 438 1933
- 403 SPITTELL J A JR, MARTIN W J AND NICHOLS D R. Bacteremia owing to gram negative bacilli. *Ann Int Med* 44 302 1956
- 404 STANLEY M M. *Bacillus pyocyaneus* infection. *Am J Med* 2 23 27 347 1945
- 405 STANLEY P C. The polymyxins (a review and comment). *Am J Med* 7 807 1949
- 406a —. SHEPHERD R G AND WHITE, H J. Polymyxins and chemotherapy. *Proc 1st Int Bull Joh Hopkins Hosp* 81 43 1947
- 407 STOJIC M AND VOJVODIC Z. Infection meningitis caused by *Pyocyanus*. *Medica kh* 9 41 1955
- 408 STOLCH W V AND SHENNER J J. Stillbirth associated with *Pseudomonas* septicemia (Report of two cases). *Am J Obst* 72 1319 1956
- 409a SUCHANOVA PLACHEROVA M. Unusual pathogenesis of edematous lesions from the family *Pseudomonas*. *Ceskoslovensk obzorn* 6 396 1957
- 407 SWIFT P H AND BLESBY S R M. Clinical aspects of the toxicity of polymyxins. *Am J Med* 110 1953
- 407a —. Antibiotic and host reaction. *Brit MJ* 1 129 1957
- 408 SYVERTON J T, HEWELL W R, KRAEHLER J ET AL. Otitis externa—clinical observation and microbiological flora. *AMA J Otolaryng* 43 212 1946

- 372 SCHIMMELBUSCH C Samml Klin Vortr Chirurgie 1890-1894 Bd 1-2 S 303
- 373 SCHLAGENHAUFER F Ueber *Pyocyanus* Infektion nach Lumbalanästhe-
sie Zentrabl Bakt 59 385 1911
- 374 SCHUMWEISER A Meningitis due to *Pseudomonas aeruginosa* following lumbar
puncture Deut Gesundheitsw 7 655 1952
- 375 SCHNEIDER H Zur Klinik und Therapie der *pyocyanus* Meningitis Wein-
klin Wchn chr 37 65 1924
- 376 SCHOENBACH E B Edward Gamahel Joneway lecture newer antibiotics
polymyxin chloromycetin and aureomycin J Mt Sinai Hosp 16 71 1949
- 377 SCHOENTAL H Nature of antibacterial agents present in *Pseudomonas*
pyocyanea cultures Brit J Exper Path 22 137 1941
- 378 SCHULTZ H W A gelatinous variant of *Pseudomonas aeruginosa* Proc Soc
Exper Biol & Med 65 289 1917
- 379 SCHULTZ W Ueber eigenartige Halskrankheiten On different throat
affections Deut che med Wchn chr 48 1495 1922
- 380 — AND JACOBOWITZ L Agranulocytosis Med Klin 21 1642 1925
- 381 SCHLERNAYER B Beiträge zur Beurteilung der Bedeutung und des Verhaltens
des *Bacillus pyocyanus* Zt chr Hyg 70 281 1895
- 381a SCHWARTZ B S WARREN M H BARKLEY F A AND LANDIS L Micro-
biological and pharmacological studies of colistin sulfate and sodium
colistin methanesulfonate Antibiotics Annual 1959-1960 New York Anti-
biotics Inc 1960 pp 41-60
- 382 SCOTT W W Blood stream infections in urology—A report of 82 cases
J Urol 21 521 1929
- 383 SEDALLIAN P LECHE J VIATEL M MARAL R AND EXBRAYAT C Meningi-
tis with multiple relapses due to *Pseudomonas aeruginosa* treated with
treptomycin intraventricularly Rev d oto neuro oph 23 487 1951
- 384 SEDILLOT C Sur la nature et les causes des suppurations bleues Gaz med
Par 5 656 1850
- 385 SENTURIA H H Etiology of external otitis Laryngoscope 55 277 1945
- 386 — CROSS R J LETT J E AND HARDY A V An evaluation of certain
therapeutic agents and procedure in the treatment of acute diffuse external
otitis Laryngoscope 64 1001 1954
- 386a SHAPIRO H A SLOAN J H AND GOLDBERG S L *Pseudomonas pyocyanus*
cholangitis Illinois MJ 114 21 1958
- 386b SHICKMAN M H GLZE, L B AND PEARCE M L Bacteremia following
cardiac catheterization report of a case and studies on the source New
England J Med 260 1164 1959
- 387 SHREWSBURY J F D B *Pyocyanus* meningitis with recovery Brit MJ
1 280 1931
- 388 SILVER C M Pelvic bone changes following suprapubic prostatectomy Bull
Hosp Joint Dis 2 10 1941
- 389 SILVERTHORPE N Meningitis in childhood Canad MAJ 48 218 1943
- 390 SIMON R D The use of fermentation reactions and pigment production to
differentiate between types of *Pseudomonas pyocyanea* and other *pseudo-*
monas species Brit J Exper Path 77 191 1956

- 427 VON SALLIMANN L. Sulfalazine as tophore-*in* Bacillus pyocyaneus infection (rab bit co nea) *Am J Ophth* 75 1922, 194
- 428 VUTLSTEKE, C. A. Met ag it soll win pinal nes the a B i M J 119 1947
- 429 WAI BREN I. A. Pa t remia fu to gram neg ti b cilli other th = Salmonella A cl n cal and therapeut c tudy A M A Arch Int M 1 83 46 1941
- 430 — The treatment of ba te l infection with th combi natio of a t b tic and gamma glob ulin *Antibiotic & Chemothe* 322, 1947
- 431 — Current co cept in th py—Neomycin polymyxin B ba it cin a d ty o b r c New En land J Med 75 8 1213 1948.
- 431 — AND HASTINGS E. V. B cterial endoc ritis du to Pseudomonas a rug a A M A Arch Path 55 418, 1943
- 432 WATTE, H. H. A contrib tion to the tudy of pyocyane u s f ection with a report of two rare e J l l e i D 542, 1908
- 433 WALKER S. H. Polymyx B in pseudomona and m t e t r i t i J Ped t 41 146 1942
- 434 WALLER TEI R S. P l myx n f i t s t eatn t of pyocy neu sep r port of a case J M t y n a Ho-p 16 190 1947
- 435 WALTHARD M. C undl en r s rothe p d Strept kokk opue pe al febe Zi b f Celurt hu G y ak 51 469 1904
- 436 WARNER P. T. J. C P l o l i t n of b t r i n i h a g f Pseudomonas pyocyanea Brit J E per Path 31 11 1940
- 437 WASSERMAN A. E per m nt lle Unte hungen ub n n s e theoret h Punkte de I mu t i leh Zi l l Hyg 263 1897
- 438 WASSERMAN M. U l r e n Epid m art u f getrete e pt h N b l I f ection N g l o e n e n B w e f die p th n t ch Wirkau keit d l l i l l u p y o y a b m m e n l l n (Epidem f eleven n e of umbl l i n f i t n of th n whor ending in death) V h w s A h F p th An t 165 342 1901
- 439 WEINE K. J. Z. K j k nd Th r g i e d P y c y n e M a g t K n d r z l Pra 20 1 1942
- 440 WEINSTEIN L. The mplicat n f ntibiotic therapy Bull New York Acad M i 91 500 1955
- 441 — AND PERRE T S. Men n t s du to Pseudomonas pyocy n a A report f th case i ted u fully with streptomycin and sulfadiazine Ann l t Med 27 103 1948
- 442 WEIN H. H. P r n ple d p a c t o f n t b i t the py New York Med cal E v l p l a I B l k ton Co 1944
- 442 — The ba t d th p r r t e A n w l n al appro ch t b ologic rel t on h p A t b i o t i c s & C l mother 7 2 1 1947
- 442b — RYD L L. W. A. AND PRICE C. W. Th f f e t of st ept m c i n b c t n p l n y m b t i p l y n y B and t eptomycin with glucuron la tone th nt t n l f f r a o f m J Am Pharm A 4 496 1940
- 443 WELLS I. C. A t b i o t i c b t a n y r d d h y Pseudomonas ac u n o Sy th of Py l h P y o l e a d P y o l l i J B l Ch m 196 331 1947
- 444 — HAYS E. E. WADE N. J. ET AL. Som b olog l p o p e t of Py l l J B l Chem 167 53 1947

- 409 TAKAHASHI A Ueber die atologische Beziehung le *Bacillus pyocyaneus* zur Geschwürbildung Dermat Ztschr Berl 71 702 1914
- 409a TEITEL M AND FLORMAN A L Postoperative endocarditis due to *Pseudomonas aeruginosa* Report of a case with recovery JAMA 172 379 1960
- 409b TENG P AND JOHNSON H A Experimental intracisternal injection of polymyxin B Its role in the treatment of septic meningitis Neurology 3 831 1953
- 409c — Experimental intraventricular and intracisternal injection of polymyxin B in the cat Neurology 3 890 1953
- 410 TERSON A (cited by Jaulin M) Sur la tuberculose de l'appareil lacrymal Thèse Paris 399 1895
- 411 THAYER W S Studies on bacterial (infective) endocarditis Johns Hopkins Hosp Reports 22 73 1926
- 412 THOMAS C I The Cornea Springfield Ill Thomas 1955 pp 416-417
- 413 THOMAS L The physiological disturbance produced by endotoxins Annual Rev Physiol 16 467 1954
- 414 THYGESON P Cited by Thomas
- 415 TILLET W S Studies on the enzymatic lysis of fibrin and inflammatory exudate by product of hemolytic streptococci Harvey Lect 43 149 1949 1950
- 416 TOMLIN C E *Pseudomonas meningitis* treated with polymyxin AMA Arch Int Med 8 863 1951
- 417 TOPLEY W W C Principles of bacteriology and immunity 4 ed (G S Wilson and A A Miles Eds) Baltimore Williams and Wilkins 1955 volume 1 pp 595-607
- 418 TRAPNELL D H *Pseudomonas pyocyaneus meningitis* successfully treated with polymyxin Lancet 766 759 1954
- 419 TRIPOLI C J Bacterial meningitis A comparative study of various therapeutic measure JAMA 106 171 1936
- 420 TROEN P AND DIAPRIO J M *Pseudomonas meningitis* treated with Terramycin US Armed Forces MJ 3 1629 1952
- 421 TURPIN R AND BOUREL M Infection à bacille pyocyanique chez un nourrisson de cinq mois Pédiatrie 3 613 1948
- 422 VALLS J PALLAZZO R AND OTTOLENGHI C E Meningitis piocyanica Rev sud am de endocrinol 11 616 1928
- 423 VAN DEN ENDE M Observation on the antigenic structure of *Pseudomonas aeruginosa* J Hyg 50 405 1952
- 424 VAUGHAN W T BECKER AND SHELTON T S Primary *Bacillus pyocyaneus meningitis* Case with recovery Arch Int Med 47 15 1931
- 424a VALCHN H C Contamination of fluorescein solution with special reference to *Pseudomonas aeruginosa* Am J Ophth 59 55 1955
- 425 VERGER I AND BENTEGRAT J Une épidémie de tétanos à bacille pyocyanique (*Pseudomonas aeruginosa*) observée dans un centre de prématurés (Epidemic of enteritis caused by a pyocyanic bacillus (*Pseudomonas aeruginosa*) observed in a premature center) Nourisson 43 141 1955
- 426 VIKLICKY J *Pseudomonas aeruginosa* as a causative agent of purulent lptomeningitis Časopis lékařský 87 1004 1948

- 427 VON SALLIMANN L. S. Had az e iontophore in Pac Illa pyocyan u inf c
tion of rat bit corn. *Am. J. Ophth* 2: 1297 1917
- 428 VUYLSTEKE C. A. Meningitis following general anesthesia. *Brit. M. J.* 1: 19
1914
- 429 WAISBREN I. A. Bacteremia due to gram negative bacilli other than Salmon
ella. A clinical and therapeutic study. *A. M. A. Arch. Int. Med.* 88: 461 1911
- 430 — The treatment of haemolytic infection with the combination of anti-toxin
and gamma globulin. *Antibiotic & Chemotherapy* 3: 197
- 431 — Current concepts in therapy—Neomycin polymyxin B bacitracin and
tyrothricin. *New England J. Med.* 258: 1213 1958
- 432 — AND HASTINGS E. V. Bacterial endocarditis due to Pseudomonas
aeruginosa. *A. M. A. Arch. Path.* 59: 718 1953
- 433 WAITE, III H. A contribution to the study of pyocyanus infection with a
report of two cases. *J. Infect. Dis.* 5: 547 1908
- 434 WALNER S. H. Polymyxin B in pseudomonas and proteus enteritis. *J. Pediat.*
41: 176 1952
- 435 WALLERSTEIN R. S. Polymyxin B in treatment of pyocyanus infection
report of a case. *J. Michigan Hosp.* 16: 190 1949
- 436 WALTARD M. F. Die endotoxogene Wirkung von Staphylococcus aureus
für Zellen. *Z. f. Infektionskrankheiten* 51: 49 1904
- 437 WARNER, P. T. J. C. P. Isolation of bacilli from Pseudomonas pyocyanus
L. *Int. J. Exp. Path.* 31: 112 1950
- 438 WASSERMAN A. Experimentell untersuchte Eigenschaften theoretische
Punkte d. Immunität. *Z. f. Infektionskrankheiten* 2: 263 1896
- 439 WASSERMAN M. Ueber die Eigenschaften der pathogenen Bakterien
des Bacillus pyocyaneus beim Menschen (Experimentelle Infektion mit
bakterieller Infektion f. die neugeborenen Kinder in der Geburt). *Virchows Arch.* 165: 342 1901
- 440 WEINE K. J. Zur Klinik und Therapie der Pyocyanus Meningitis. *Kinder*
ärzt. Praxis 15: 119 1907
- 441 WEINSTEIN L. The implications of antibiotic therapy. *Bull. New York Acad.*
Med. 31: 500 1955
- 442 — AND PERRIN T. S. M. Induced to Pseudomonas pyocyanus. A report
of three cases treated successfully with streptomycin and sulfadiazine. *Ann.*
Int. Med. 29: 103 1948
- 443 WELCH H. P. Principles and practice of antibiotic therapy. New York. Medical
Encyclopedia Inc. Bl. E. T. Co. 1954
- 444a — The host and the parasite. A new biological approach to the relationship
Antibiotics & Chemotherapy 7: 111
- 444b — PANDALL W. A. AND PRICE C. W. The effect of streptomycin bacitracin
polymyxin combination polymyxin B and streptomycin with glucanase on
the virulence of man. *J. Am. Pharm. Ass.* 31: 486 1950
- 445 WELLS I. C. Antibiotic resistance produced by Pseudomonas aeruginosa
Synthesis of Py. I. Py. I. d. Py. III. *J. Pharm. Chem.* 196: 331 19
- 446 — HAYS E. E. WADE N. J. ET AL. Synthesis of Py. II
J. Biol. Chem. 16: 53 1947

- 441a WESSINCK F VAN FLAKUM H W AND RENAUD H The prevention of *Pseudomonas aeruginosa* infections in irradiated mice and rats *Radiation Re* 7 491 1957
- 441b WIDERNIAN A A fatal case of meningitis due to *Pseudomonas aeruginosa* following upper respiratory infection *J Albert Einstein Med Center* 2 31 1953
- 446 WIGGINS H L Experimental studies on the eye with polymyxin B with discussion by Allen and Braley *Am J Ophthalm* 35 83 1952
- 447 WILLIAM H G AND OVENS J M Pyogenic liver abscesses with recovery *Am J Surg* 62 412 1943
- 448 WILLIAMS E P AND CAMEROV K Upon general infection by the *Bacillus pyocyaneus* in children *J Path & Bact* 3 344 1896
- 449 WILLIAMS H K HENCH M E AND GUERRY D 3RD *Pyocyanus* ulcer—Clinical report and experimental investigation *Am J Ophthalm* 37 538 1954
- 450 WILLIAMS R P Symposium on bacterial pigment *Bact Rev* 20 282 1956
- 451 WINDLE W F Activities of certain bacterial polysaccharides *Tr New York Acad Sc* 14 159 1952
- 452 — CHAMBERS W W RICKER W A ET AL Reaction of tissue to administration of a pyrogenic preparation from a *pseudomonas* species *Am J Microsc* 219 422 1950
- 453 WISE R A AND MUSSER J H *Bacillus pyocyaneus* meningitis—Report of six cases *New Orleans M & S J* 97 145 1939
- 454 WISE R I SHAFFER J M AND SPINK W W The syndrome of vascular collapse due to gram negative bacilli—its management with L norepinephrine and antibiotics *J Lab & Clin Med* 40 961 1952
- 455 WOLLSTEIN M Ulcerative gastritis and general infection with the *Bacillus pyocyaneus* *Childr Arch Pediatr* 14 760 1897
- 456 WREDE F Über das Pyocyanin den blauen Farbstoff des *Bacillus pyocyaneus* *Ztschr Hyg* 111 90 1930
- 456a WRIGHT W W AND WELCH H Chemical biological and clinical observations on colistin *Antibiotics Annual 1959-1960* New York Antibiotics Inc 1960 pp 61-74
- 456b WRIGHT S S POTEE K C AND FINLAND M Susceptibility of *pseudomonas* to ten antibiotics in vitro. Some properties of recently isolated strains *Am J Clin Path* 24 1121 1954
- 457 WUKETICH S Metastatic necrotic thyroiditis by *Pseudomonas pyocyaneus* *Virchows Arch F path Anat* 329 267 1956
- 458 YAWN E SCHREIBER M HARDY A V AND MITCHELL H B Otitis externa *Project Report USAF School of Aviation Med* Nov 1953
- 459 YOUNG C Inhibition production and antibiotic activity in cultures of *Pseudomonas aeruginosa* *J Bact* 54 109 1947
- 460 YOW E M Development of proteus and *pseudomonas* infections during antibiotic therapy *JAMA* 149 1184 1952
- 461 — AND MOYER J H Toxicity of polymyxin B Human studies with particular reference to evaluation of renal function *AMA Arch Int Med* 92 249 1953

- 462 ——— AND TOWNSEND E. S. Observation on an extract possessing potent proteolytic activity derived from *Limulus aeruginosa*. *Am J Med* 14: 162 1953 (Abstract)
- 463 ZAHL, P. A. AND HUTNER S. H. *Biology of py* T New York: Academic Press 1957
- 464 ——— AND ——— Temperature factors in the action of certain bacterial endotoxins. *Proc Soc Exper Biol & Med* 56: 156 1944
- 465 ZIMMERMAN O. Die Pyocyane 3—Meningitis beim Neugeborenen und jungen Säugling. *Ann paedat* 179: 198 1949

- 444a WENSINCK F VAN BERAUM H W AND RENAUD H The prevention of *Pseudomonas aeruginosa* infections in irradiated mice and rats *Radiation Res* 7 491 1957
- 445 WIDERMAN A A fatal case of meningitis due to *Pseudomonas aeruginosa* following upper respiratory infection *J Albert Einstein Med Center* 2 31 1953
- 446 WIGGINS R L Experimental studies on the eye with polymyxin B with discussion by Allen and Braley *Am J Ophth* 35 83 1952
- 447 WILLIAM H G AND OVENS J M Pyogenic liver abscesses with recovery *Am J Surg* 62 412 1943
- 448 WILLIAMS H P AND CAMERON K Upon general infection by the *Bacillus pyocyaneus* in children *J Path & Bact* 3 344 1896
- 449 WILLIAMS R K HENCH M E AND GLERRY D 3rd *Pyocyanus* ulcer—Clinical report and experimental investigation *Am J Ophth* 37 538 1954
- 450 WILLIAMS R P Symposium on bacterial pigment *Bact Rev* 20 282 1956
- 451 WINDLE W F Activities of certain bacterial polysaccharide *Tr New York Acad Sci* 14 159 1952
- 452 — CHAMBERS W W RICKER W A, ET AL Reaction of tissues to administration of a pyrogenic preparation from a *pseudomonas* species *Am J Micro* 219 422 1950
- 453 WISE R A AND MESSER J H *Bacillus pyocyaneus* meningitis—Report of six cases *New Orleans M & SJ* 92 145 1939
- 454 WISE R I SHAFFER J M AND SPINK W W The syndrome of vascular collapse due to gram negative bacilli—its management with L norepinephrine and antibiotics *J Lab & Clin Med* 40 961 1952
- 455 WOLLSTEIN M Ulcerative gastritis and general infection with the *Bacillus pyocyaneus* *Childr Arch Pediatr* 11 760 1897
- 456 WREDE F Über das Pyocyanin den blauen Farbstoff des *Bacillus pyocyaneus* *Ztchr Hyg* 111 90 1930
- 456a WRIGHT W W AND WELCH H J Chemical biological and clinical observations on colistin *Antibiotics Annual 1959-1960* New York: Antibiotics Inc 1960 pp 61-74
- 456b WRIGHT S S POTER K G AND FINLAND M Susceptibility of *pseudomonas* to ten antibiotics in vitro. Some properties of recently isolated strain *Am J Clin Path* 24 1121 1954
- 457 WUNETICH S Metastatic necrotic thyroiditis by *Pseudomonas pyocyaneus* *Virchows Arch F path Anat* 329 267 1956
- 458 YAWN E SCHREIBER M HARDY A V AND MITCHELL R B Otitis externa *Project Report USAF School of Aviation Med* Nov 1953
- 459 YOLAC G Pigment production and antibiotic activity in culture of *Pseudomonas aeruginosa* *J Bact* 54 109 1947
- 460 YOW E M Development of proteus and *pseudomonas* infections during antibiotic therapy *JAMA* 149 1184 1952
- 461 — AND MOYER J H Toxicity of polymyxin B Human studies with particular reference to evaluation of renal function *AM J Arch Int Med* 92 418 1953

- 462 ——— AND TOWNSEND F S Observations on an extract possessing potent proteolytic activity derived from *Isa idomina ariginosa* Am J Med 14 67 1953 (Abstract)
- 463 ZAHLE P A AND HILTZER S H Biology of *Pyrgon* Tr New York Acad Sci 14 161 1952
- 464 ——— AND ——— Temperature factors in the action of certain bacterial endotoxins Proc Soc Exper Biol & Med 56 126 1943
- 465 ZIMMERMAN O De Pyocyaneus—Meningitis beim Neugeborenen und jungen Säugling Ann Jahrbst 172 198 1919

- 444a WENSINCK F VAN BEKKUM III W AND RENAUD H The prevention of *Pseudomonas aeruginosa* infections in irradiated mice and rats Radiation Res 7 491 1957
- 445 WIDERMANN A A fatal case of meningitis due to *Pseudomonas aeruginosa* following upper respiratory infection J Albert Einstein Med Center 2 31 1953
- 446 WIGGINS R L Experimental studies on the eye with polymyxin B with discussion by Allen and Braley Am J Ophth 33 III 1952
- 447 WILLIAM H G AND OVENS J M Pyogenic liver abscess with recovery Am J Surg 62 412 1913
- 448 WILLIAMS E P AND CAMERON K Upon general infection by the *Bacillus pyocyaneus* in children J Path & Bact 3 344 1896
- 449 WILLIAMS R K HENCH M E AND GUERRY D 3RD *Pyocyanus* ulcer—Clinical report and experimental investigation Am J Ophth 37 538 1954
- 450 WILLIAMS H P Symposium on bacterial pigment Bact Rev 20 282 1956
- 451 WINDLE W F Activities of certain bacterial polypeptides Tr New York Acad Sc 14 159 1952
- 452 — CHAMBERS W W RICKER W A ET AL Reaction of tissues to administration of a pyrogenic preparation from a *Pseudomonas* species Am J Micro 219 422 1950
- 453 WIRE R A AND MÜSSER J H *Bacillus pyocyaneus* meningitis—Report of six cases New Orleans M & S J 92 145 1939
- 454 WISE R I SHAFFER J M AND SPINK W W The syndrome of vascular collapse due to gram negative bacilli—its management with L norepinephrine and antibiotics J Lab & Clin Med 40 961 1952
- 455 WOLLSTEIN M Ulcerative gastritis and general infection with the *Bacillus pyocyaneus* Childr Arch Pediatr 14 760 1897
- 456 WRIDE F Über das *Pyocyanin* den blauen Farbstoff des *Bacillus pyocyaneus* Ztschr Hyg. 111 90 1930
- 456a WRIGHT W W AND WELCH H Chemical biological and clinical observations on colistin Antibiotics Annual 1959–1960 New York Antibiotics Inc 1960 pp 61–74
- 456b WRIGHT S S POTEE K G AND FINLAND M Susceptibility of *Pseudomonas* to ten antibiotics in vitro Some properties of recently isolated strain Am J Clin Path 24 1121 1954
- 457 WLNETICH S Metastatic necrotic thyroiditis by *Pseudomonas pyocyanea* Virchow Arch F path Anat 379 267 1956
- 458 YAWN III SCHREIBER M HARDY A V AND MITCHELL, R B Otitis externa Project Report USAF School of Aviation Med Nov 1953
- 459 YOUNG C Pigment production and antibiotic activity in culture of *Pseudomonas aeruginosa* J Bact 54 109 1947
- 460 YOW E M Development of proteus and *Pseudomonas* infection during antibiotic therapy JAMA 149 1184 1952
- 461 — AND MOYER J H Toxicity of polymyxin B Human subject with particular reference to evaluation of renal function AMA Arch Int Med 92 248 1953

REFERENCES

462. ——— AND TOWNSEND E. N. Observations on an extract from
proteolytic action derived from *Pseudomonas aeruginosa*
1476, 1933 (Abstr.) 32
72
463. ZARL, P. A. and HILTZ, S. H. Properties of *proteolytic* *Trichoderma*
14161 1934
464. ——— AND ——— Temperature factor in the action of *proteolytic* *Trichoderma*
toxins. *Proc. Soc. Exper. Biol. & Med.* 26: 136, 1934. 13
465. ZIMMERMAN O. The Protease — Menages & *Trichoderma*
Saunders Company, ed. 1938, 1940 30

- 444a WENSINCK F VAN BEKKUM D W AND RENALD H The prevention of *Pseudomonas aeruginosa* infections in irradiated mice and rats *Radiation Res* 7 491 1957
- 445 WIDERMANN A A fatal case of meningitis due to *Pseudomonas aeruginosa* following upper respiratory infection *J Albert Einstein Med Center* 3 31 1953
- 446 WIGGINS R L Experimental studies on the eye with polymyxin B with discussion by Allen and Braley *Am J Ophth* 35 83 1952
- 447 WILLIAM H G AND OVENS J M Pyogenic liver abscesses with recovery *Am J Surg* 62 412 1943
- 448 WILLIAMS E P AND CAMERON K Upon general infection by the *Bacillus pyocyaneus* in children *J Path & Bact* 3 344 1896
- 449 WILLIAMS P A HENCH M E AND GUERRY D 3RD *Pyocyaneus* ulcer—Clinical report and experimental investigation *Am J Ophth* 37 538 1954
- 450 WILLIAMS R P Symposium on bacterial pigments *Bact Rev* 20 282 1956
- 451 WINDLE W F Activities of certain bacterial polysaccharides *Tr New York Acad Sc* 14 159 1952
- 452 — CHAMBERS W W RICKER W A ET AL Reaction of tissues to administration of a pyrogenic preparation from a *pseudomonas* species *Am J M Sc* 219 422 1950
- 453 WISE R A AND MUSSLER J H *Bacillus pyocyaneus* meningitis—Report of six cases *New Orleans M & SJ* 92 145 1939
- 454 WISE R I SHAFFER J M AND SPINK W W The syndrome of vascular collapse due to gram negative bacilli—its management with L norepinephrine and antibiotic *J Lab & Clin Med* 40 961 1952
- 455 WOLLSTEIN M Ulcerative gastritis and general infection with the *Bacillus pyocyaneus* *Childr Arch Pediatr* 14 760 1894
- 456 WREDE F Über das Pyocyanin den blauen Farbstoff des *Bacillus pyocyaneus* *Zt chr Hyg* 111 90 1930
- 456a WRIGHT W W AND WELCH H Chemical biological and clinical observations on colistin *Antibiotics Annual 1959-1960* New York: Antibiotics Inc 1960 pp 61-74
- 456b WRIGHT S S POTEE A G AND FINLAND M Susceptibility of *pseudomonas* to ten antibiotics in vitro Some properties of recently isolated strain *Am J Clin Path* 24 1121 1954
- 457 WUKETICH S Metastatic necrotic thyroiditis by *Pseudomonas pyocyanea* *Virchow Arch F path Anat* 329 967 1956
- 458 YAWN H SCHREIBER M HARDY A V AND MITCHELL, K B Otitis externa *Project Report USAF School of Aviation Med* Nov 1953
- 459 YOUNG G Pigment production and antibiotic activity in cultures of *Pseudomonas aeruginosa* *J Bact* 54 109 1947
- 460 YOW E M Development of *potens* and *pseudomonas* infection during antibiotic therapy *JAMA* 149 1184 1952
- 461 — AND MOYER J H Toxicity of polymyxin B Human studies with particular reference to evaluation of renal function *AMA Arch Int Med* 92 248 1953

Index

Abc
of abdominal area 9 18
of axilla 9
of bronchus 37
of costal muscle 52
of esophagus 38
of gallbladder 49
of heart 49
of iliopectineal muscle 5
of ischiofemoral space 63
of kidney 45 46 50 5
of liver 30 50 63
of lung 14 36 37 49 50
of mesentery 53
of mesenteric 52
metastatic 50 63
of middle ear 49 63
of parotid gland 63
of peritoneum 63
of pleura 37 49
of prostate gland 45
of renal pelvis 50
of spleen 49
of uhepatic 63
sulphuric 63
of testis 63
of testis 40
of thyroid gland 61 63
of tonsil 67
Adrenal cortex 37 2 13
Aerobically 17
Artery 36 66
Agitation 3
Agranulocyte 9 11 12
Antibacterial 3
Antibiotic (see Antimicrobial agent)
Antibody 3
Antimetabolite 10 11 13-15 18
37 33 35 37 39 41 43 45
47 51 55 66 71 73
Appendix 41-43
Arginine 11 13
Arginine 23
Arginine 23
Artificially 13 63
Artificially 13 3 63
Artificially 50 67
Artificially 38
Artificially 21 30
Bacillus anthracis 1
Bacillus anthracis 1
Bacterial infection 11
Bacterial infection 12 15 18 19
Bacterial infection 10 79
Bacteriophage 79
Bile acid
Bile acid
arteriovenous fistula 14 13
arteriovenous 63
lesion of 7
arteriovenous 37
arteriovenous 37
arteriovenous 8
Bone marrow 9 11 13 15 17
Bronchial 1
Bronchitis 37 38
Bronchitis 37 38
Burn 18 19 51 66
Burn 51
Cancer 18 40 43 50 53 72
Cancer 3 4 66
Catheter 43
Cellulitis 16 18 69
Cholera 63
Cholera 63
Colon 28 30 4
Colon 6-68 72 73
Colon 40 43
Colon Mycobacterium 11
Colon Mycobacterium 11
Colon Mycobacterium 22 23 30

- Intestinal tract (see Gastrointestinal in feet on)
 Ichiecthalabce 63
 Jaundice 9 39 41 42
 Joints (see Arthritis)
 Leucocidin 11
 Leukemia acute 4 11 1 36 58 73
 L. ukocyto 7
 Leukopenia 9 11 41 48 72
 Lymphodinitis 61
 Maladepycyca 6
 Marrow (see Bone marrow)
 Maltol 22 31 63
 Metastinalabce 52
 Meningitis 13 19-36 40 48 49 54 63 66
 Metastalarre 63
 Monia (see Canis alban)
 Mortality 20 3
 Muscle paralysis of 6
 Myocarditis 49
 Oribis 4
 Otispl 53 54 56
 Osteomyelitis 50-59
 Otis externa 60 63 66
 Otis media 26 8 9 56 60 63
 Pillary cerebro 50
 Paratyphoid fever 7
 Parotiditis 63
 Pathogenicity 1 6 71
 Pathogen 69 70
 Pericarditis 49 63
 Perinfectalitis 45
 Peritonitis 63
 Petichiae 17
 Phagocytes 73
 Phlebotomy 37 50 63
 Pigment 2
 Pionin 1
 Pleurisy 36 37
 Pseudomycetozoa intestinal 43
 Pneumonia 36 38
 Polymyxin B 10 11 15 18, 19 25-33 38 41 43 51 59 64-67 72
 Portal of entry
 bone marrow 69
 cytotoxicity 11
 gastrointestinal tract 9 10 13 30 31 42 44
 genitourinary tract 9 11 13 14 30 31 43-50
 instrumentation, 10 20 22, 37
 middle ear 9 11 69
 operative procedure 9 10 20
 pneumoencephalography 20
 respiratory tract 10 14 69
 skin 9 13 69
 spinal fluid, 26 25-32 69
 umbilical cord 9
 Pregnancy 13 28 29 31 32, 47 50
 Products of Pseudomonas
 antitoxic 3
 enterotoxins 1 7 59 72
 enzyme 12
 fluorescence 2 33
 pigment 2
 toxin 7 50
 Propidium 73
 Icterus 45
 Proteolytic activity 1 12
 Pseudomonas aeruginosa 1
 Pseudomonas procyan, 1
 Puerperal infection 47
 Pulmonary infection (see Respiratory tract infection)
 Pupa 9
 Pycnonephritis 40 46 50 5
 Pyemia 5
 Pyocyanin 2
 Pyoniferous 45
 Pyrogen 2
 Pyromen (see Pyronin)
 Renal abscess 4
 Respiratory tract infection 36-39
 abscess 38
 bronchiectasis 37 38
 bronchitis, 37 38

- Cutaneous lesions (*see* Skin)
- Cyanopyaemia 6
- Cyano is 10 36 39 41 48 49
- Cystitis 45 46
- Cytochrome oxidase 1
- Dental caries 63
- Diarrhea 39 41-43 49 66
epidemic diarrhea of the newborn 39
" 42 66 68
- Dysuria 47
- Ear infection 60
otitis externa 60 63 66
otitis media 63
- Ecthyma gangrenosum 11 15 19 13 69
- Empyema 29 36 37 49 67
- Endocarditis (*see* Bacterial endocarditis)
- Endometritis 47 48
- Endotoxins 1 2 7 39 72
- Enteritis 36 39-43 48 53
- Enzyme 2 12 35 60 67
- Epidemic diarrhea of the newborn (*see* under Diarrhea)
- Epidemic 4 7
- Epidemiology 3 4 8 9 20-22 41 47
60 71 72
- Epididymitis 43
- Epiglottic abscess 38
- Etiology 40 43 63
- Eye infections 59 60
conjunctivitis 59
corneal ulcer 59 66
dacryocystitis 59
endophthalmitis 60
meibomitis 60
panophthalmitis 59
punctate keratitis 59
- Fever 6 7 10 11 39 43 44 47-50
58, 72
- Febrile therapy 1
- Fibrocystic disease of pancreas association with 37
- Fingertail infection 18
- Fluorescence 2 33
- Furunculosis 52
- Gamma globulin 72 13
- Gastrointestinal infection 3 39-43 52
appendicitis 41 43
cholera 63
cholecystitis 63
colitis 40 13
diarrhea 9 39 41-43 49 66
enteritis 39-43 48
epiglottic abscess 38
esophagitis 40 13 63
hepatic abscess 63
peritonitis 63
- Genitourinary infection 10 11 28 43-47 65
circumcision 28 30 45
cystitis 45 46
epididymitis 45
orchitis 45
papillary necrosis 50
perinephritic abscess 45
prostatitis 45
pyelonephritis 46 50 52
pyonephrosis 45
- Granulocytopenia 11-12
- Hemorrhage 6 11 17
into adrenal 50
into local tissue 69
- Hepatic abscess 63
- Hepatomegaly 10
- Histology 7 69 70
of blood vessels 7
of skin 7
- Hydrocephalus 22 3 48
- Hypotension 41 50 72
- Icterus (*see* Jaundice)
- Iliopsoas abscess 52
- Immunology 3
antibodies 3
antitoxins 3
- Incidence 3 9 21 35 45 69
- Infarction 3

- empyema 36 37 49 67
 lung abscess 36 47
 pleuritis 37
 tracheitis 38
- Sapirivitan 13
 Schwartzman phenomenon 72
 Sensitivity study 33 72
 Septicemia 4 6-11 18 19 36 39 41
 44-46 49 52 59 65
 Serology 3
 Shanghai fever 7
 Skin lesion (*see also* Burn) 7 9 10
 11 15-19 39 43 48 49 51 2
 Spinal drainage 23 30
 Spinal fluid
 characteristics of 32
 contamination of 21 27
 Splenomegaly 7 9 10 15
 Streptokinase streptolysin 25 26
 30 66
 Subhepatic abscess 63
- Suppurative abscess 63
 Sulfonamides (*see* Antimicrobial agent)
 Synovitis 58 59
- Thrombocytopenia 9 12
 Thrombophlebitis of lateral sinus 63
 Thrombosis 37 63 69
 Thyroid abscess 63
 Thyroiditis 61 63
 Tonillitis 62
 Toxin 7 59
 Tracheitis 38
 Typhoid fever 7 28 39 43
- Umbilical infection 7 9 28 29 31 53
 Uremia 46
- Vaccinosis 8 34 62 63 69
 Vasomotor effect 6
 Virulence 9
- X irradiation 4 39 71

